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A STUDY OF THE LESIONS IN THE VASCULAR SYSTEM IN FATAL CASES OF CHRONIC NEPHRITIC TOXÆMIA OF PREGNANCY

MALIGNANT NEPHROSCLEROSIS[1]

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THE toxæmias of pregnancy present a series of problems which are of the utmost importance. These have been attacked from a variety of viewpoints including the study of the histopathological lesions, the chemical and metabolic changes, and the clinical aspects. None of these studies can be completely satisfactory without information as to etiology, and this is entirely lacking. However, material is accumulating which is adding much to the understanding of the processes. It is the purpose of this paper to present observations on the lesions in the vascular systems of those patients who have been injured by pregnancy toxæmias and who have eventually died after a typical clinical course. These lesions have not been adequately described in relation to pregnancy toxæmias but have received much attention in other conditions under the term malignant nephrosclerosis by Volhard and Fahr (1914), Fahr (1934), Schuermann and MacMahon (1933), and others. A study of the literature shows that the frequency with which this condition occurs in relation to pregnancy toxæmias has been overlooked. Descriptions of the so called obstetrical chronic nephritis also lack a realization of the similarity of the two conditions.

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The material is that obtained at autopsy on patients who have died on the obstetrical service of Johns Hopkins Hospital. It does not represent in any way the total incidence of the condition, since the vast majority of the women who die of chronic nephritis following a pregnancy toxæmia do not return to the obstetrical service at this time. For completeness, consideration was given to the histories of all patients who were indexed as having died of nephritis. The material from all upon whom autopsies had been done was obtained and, wherever possible, the kidney, adrenal, and pancreas were studied. To the usual staining procedures were added the connective tissue stain of Mallory and the elastic tissue stain of Verhoeff.

This study does not include the deaths from eclampsia. As will be seen, it does include in so far as autopsy material allowed, all other deaths in which kidney lesions were clinically suspected. Two groups of material emerged. There was, first, that group in which a pregnancy toxæmia had occurred, hypertension had persisted postpartum, and, after a varying period of time, uræmic death had ensued. This group constitutes the subject of the present study.

Brief consideration has also been given to

the second group studied. In these patients, we have no history of prolonged severe hypertension and the condition may be considered as acute and of short duration. These have been included for comparison and for the purpose of stressing the fact that there is an essential histological difference between the lesions of the acute toxæmias of pregnancy and those which may ultimately lead to the death of the individual concerned. A difference in etiology or mechanism of production is not implied.

In 1927, a toxæmia clinic was established at Johns Hopkins Hospital with the object, not only of giving special attention to those patients who show toxæmias during pregnancy, but also of following these patients after delivery for treatment and for the collection of data. This clinic has yielded valuable information, particularly as to the ultimate prognosis for those patients upon whom a diagnosis of chronic nephritis following a pregnancy toxæmia has been made. This will be considered below. It has also served to focus attention upon the end stages of the disease, and is steadily producing more and more material for study of the condition.

It should be stated that the term chronic nephritis is used here in the sense employed by Stander and Peckham (1926) in their classification of the toxæmias of pregnancy. This diagnosis is made during pregnancy when the blood pressure rises above 155 millimeters mercury systolic and/or 100 millimeters mercury diastolic, with or without albuminuria and in the absence of signs and symptoms of pre-eclampsia. The previous history and the blood chemistry findings, the type and degree of the urinary findings, and the physical examination with special attention to the eye grounds will temper the diagnosis. Peckham and Stout (1931) showed that one-fifth of the patients so diagnosed showed no demonstrable damage at subsequent examinations. On the other hand, one-fourth of those diagnosed as of the low reserve kidney or pre-eclamptic type during pregnancy and the early puerperium were shown to have residual damage later. The immediate clinical diagnosis then is a loose one and must be controlled by prolonged observation after delivery. This gives the second set of criteria for the diagnosis of chronic nephritis. The presence of a persistent hypertension of 150 millimeters mercury systolic and/or 100 millimeters mercury diastolic and/or a persistent albuminuria postpartum (Peckham and Stout, 1931) allows such a diagnosis, while the absence of any of these makes it unlikely that the original toxæmia has been of the chronic nephritic type.

Such a follow-up will yield surprising information. Peckham (1931) has shown that of 74 eclamptics so observed, 23 per cent showed ultimate evidence of chronic nephritis. Of the toxæmic patients, excluding those with pernicious vomiting and eclampsia, 40 per cent showed residual damage. Some of these latter, however, were known chronic nephritics before the present pregnancy, so that the incidence here expressed is not a proper expression of the incidence relation. But these figures do serve to point out the frequency with which permanent damage to the woman follows the toxæmias of pregnancy. It should be pointed out that this is at variance with the observations of Heynemann (1924), Fahr (1924), Zondek and co-authors (1924), and Nevermann (1927) as reported by Bell (1932).

The next step is to consider what eventually happens to these women with chronic nephritis. Stander and Peckham (1931) reported on 135 women who had a chronic nephritic toxæmia of pregnancy and who had been observed on the obstetrical service of the Johns Hopkins Hospital during pregnancy one or more times over a period of from 1 to 11 years previously. They found that 46 were dead and of these, 37 had died of clinical nephritis. Of those alive, 26 showed no evidence of permanent cardiovascular-renal damage (the one-fifth error referred to above) while 30 had evidence of a severe chronic nephritis, and 20 showed signs of moderate chronic nephritis. Of the remainder, no information was obtained.

It is shown then that this sequence of events; toxæmia of pregnancy, chronic nephritis, and ultimate early death, occurs with striking frequency. A causal relation might be presumed but is not established. It would seem that a careful histological study of the steps in the process might yield valuable information.

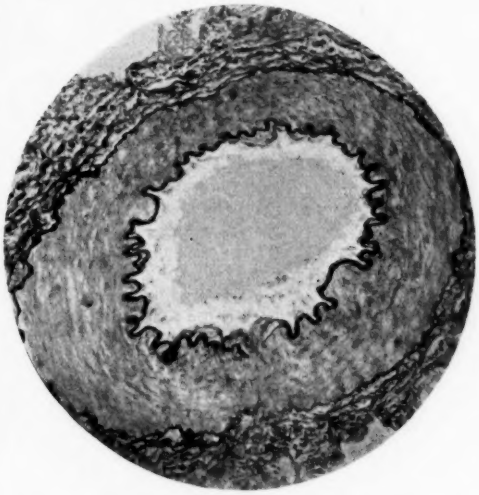

Fig. 1. Interlobar artery showing vascular hypertrophy. Note particularly the thick muscular media. (Verhoeff's elastic tissue—Van Gieson connective tissue stains.) ×88.

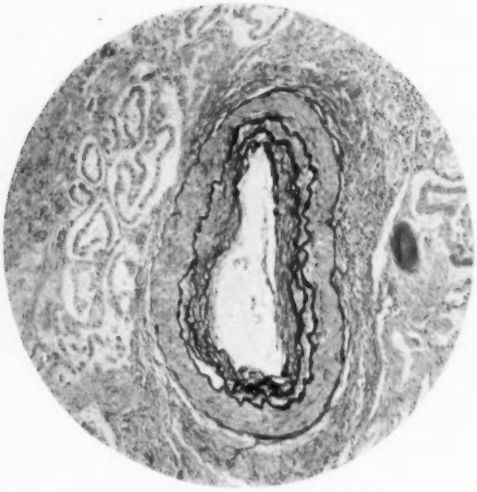

Fig. 2. Arcuate artery, showing vascular hypertrophy. The media is thickened and well preserved. There is a connective tissue thickening of the intima and a well developed lamellar elastosis. (Verhoeff's elastic tissue—Van Gieson connective tissue stains.) ×88.

Until recently this was confined to a consideration of the lesions of eclampsia. The work of Zangemeister in directing attention to the tissue œdema and its extrarenal cause as a fundamental condition, and of Hinselmann (1921, 1924) in the study of capillary spasm, are too well known to require comment. The work of Volhard and Fahr on the kidney gave a new impetus to the study of that organ in the toxæmias. Their division of kidney disease into nephritis, nephrosis, and sclerosis clarified the obstetrical problems. Volhard (1918) pointed out that the kidney lesions seen in the toxæmias of pregnancy and particularly in eclampsia are not primarily degenerative but show a typical ischæmia of the glomeruli with marked secondary parenchymal changes. This directed attention once more to the vascular system. Heynemann (1920, 1921) took issue with this, described the lesions of the toxæmias as a whole as degeneration in the glomerulus and the convoluted tubules and coined the term "pregnancy glomerulonephrosis" to describe it. He was careful to point out, however, that when blood appears in the urine or the systolic blood pressure goes above 165 or 175 millimeters mercury, or when the blood pressure remains elevated following preg-

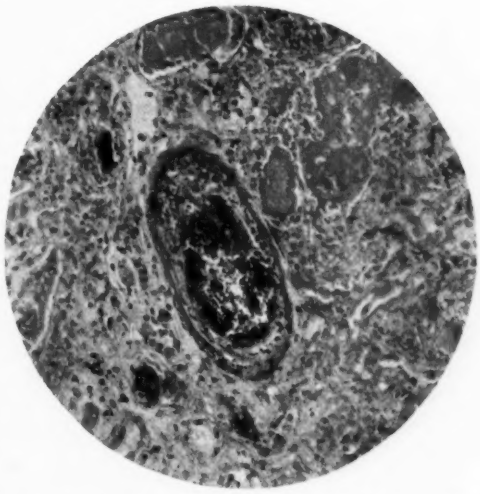

Fig. 3. Lobular artery showing vascular hypertrophy with a connective tissue thickening of the intima; the internal elastic lamina is stretched, and the outer muscular media still partially intact is narrow. Superimposed on this older process is a recent change with saturation of the intima with blood, partial thrombosis, focal disappearance of internal elastic lamina, and hæmorrhage into the media and adventitia. (Hæmatoxylin and eosin.) ×140.

Fig. 4. Lobular artery, with branching afferent arteriole. There is vascular hypertrophy, connective tissue thickening of the intima, a deposition of fluid-like ground substance beneath the endothelium, swelling of the endothelial cells, and collapse of the lumen. The muscular media in places is still easily recognizable. The smaller branches show occlusion of their lumina, thrombosis, and a saturation of their walls with plasma and fibrin. (Hæmatoxylin and eosin.) ×105.

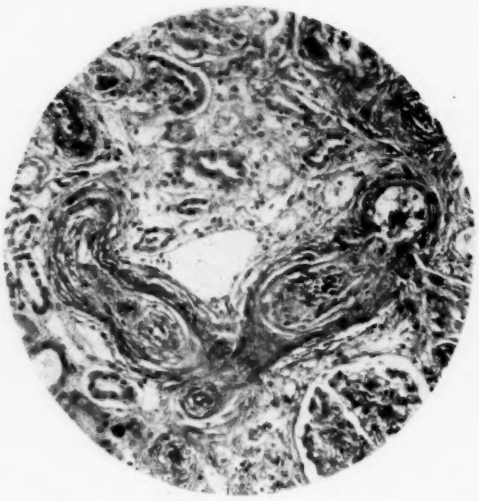

Fig. 5. Small lobular arteries. The adventitia is thickened, the media is largely replaced by connective tissue. One of the vessels shows a fusiform swelling of the basement membrane. There is a mucoid thickening of the intima, with few cells and an abundance of mucinous intercellular ground substance. The lumina are greatly narrowed. The endothelial cells are swollen. In such vessels one may trace the incorporation of endothelial cells into the underlying ground substance. (Hæmatoxylin and eosin.) ×105.

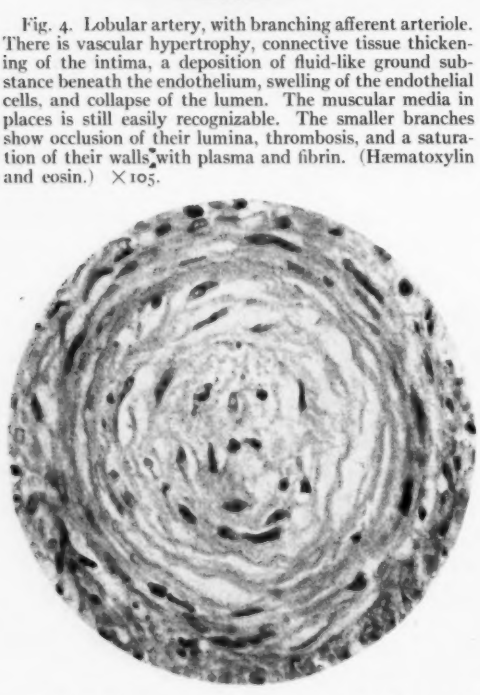

Fig. 6. Lobular artery, showing hypertrophy. The muscle fibers of the media are large, stretched, and not easily recognizable. Internal elastic lamina stretched but intact. Lumen apparently obliterated due to great thickening of intima. In this thickened intima are concentric lamellæ of cells, mucoid intercellular substance, newly formed elastic fibrils, scattered endothelial cells. (Hæmatoxylin, eosin.) ×315.

nancy, the condition is likely to be a glomerulonephritis with proliferative lesions in the glomerulus as described by Volhard (1918). No attention was given by either of these authors to the vessels of the kidney other than the afferent arteriole and the capillaries of the glomerular tuft.

Many other investigators have examined and reported upon the kidney lesions of the various toxæmias. Among these Bell (1932) describes a series in which pregnancy had occurred in the presence of pre-existing kidney disease. The microscopic findings are incomplete, and his conclusion is that the kidneys show "typical advanced chronic glomerulonephritis." Baird and Dunn (1933) also describe 5 cases of chronic nephritic toxæmia with similar conclusions. Neither has given attention to the arteriolar lesions. Russel (1929) described similar lesions in a group which she designates "toxæmias of pregnancy other than eclampsia." A search of the literature has revealed no complete description of the vascular lesions of those women who have

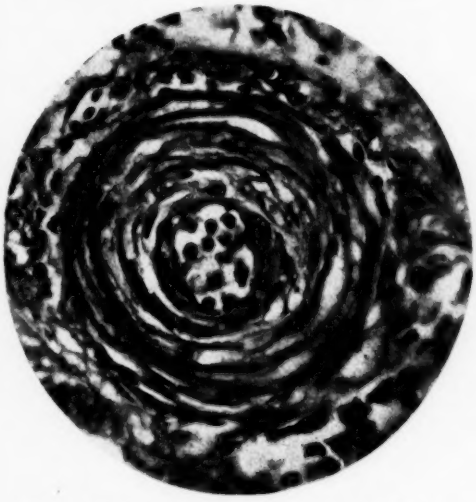

Fig. 7. Lobular artery showing hypertrophy. The muscle fibers of the media are large, stretched, and indistinct. The internal elastic lamina is thick and granular. The intima is greatly thickened by concentric lamellæ of spindle shaped cells and intercellular fibrils embedded in a mucoid ground substance which near the lumen contains plasma and fibrin. Endothelial cells swollen and indistinguishable from underlying cells in ground substance. Leucocytes within lumen. (Hæmatoxylin and eosin.) ×585.

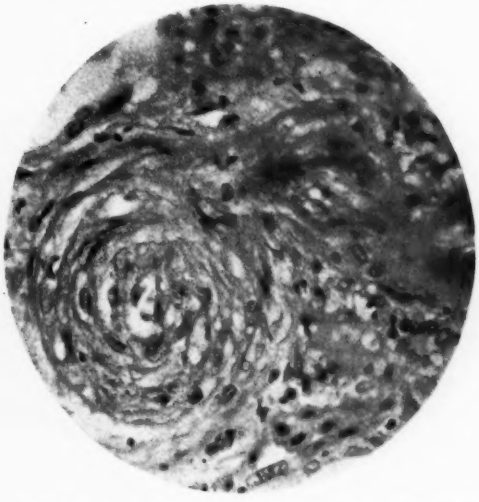

Fig. 8. Lobular artery with small afferent arteriole. The lobular artery is almost completely transformed into concentric lamellæ of cells and intercellular fibrils embedded in a mucoid ground substance. The lumen is apparently obliterated. The endothelial cells are swollen and may be traced into the underlying ground substance. The wall of the small afferent arteriole is saturated with plasma and fibrin. (Hæmatoxylin and eosin.) ×350.

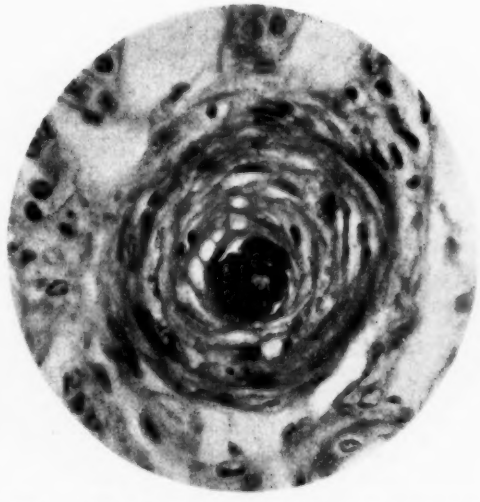

Fig. 9. Lobular artery. The muscular media is replaced by connective tissue. The intima is greatly thickened by concentric lamellæ of spindle shaped cells and intercellular fibrils, embedded in a vacuolated mucoid ground substance. The lumen is obliterated by a small fibrin thrombus. (Hæmatoxylin and eosin.) ×350.

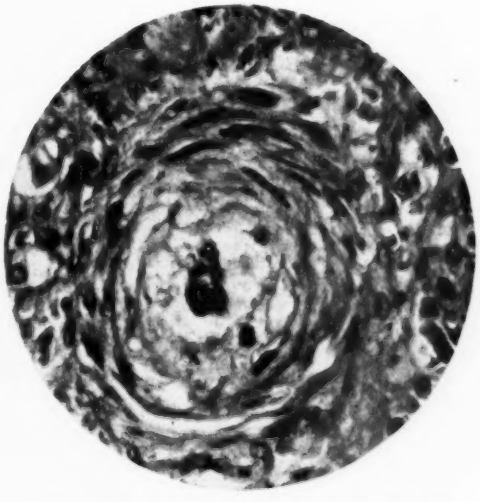

Fig. 10. Small lobular artery. Muscle fibers of media still recognizable; they are hypertrophied. The thickened intima is largely composed of a mucoid ground substance in which few cells and delicate fibrils may be seen. Endothelial cells are swollen and stain intensely. Lumen collapsed and nearly obliterated. (Hæmatoxylin and eosin.) ×425.

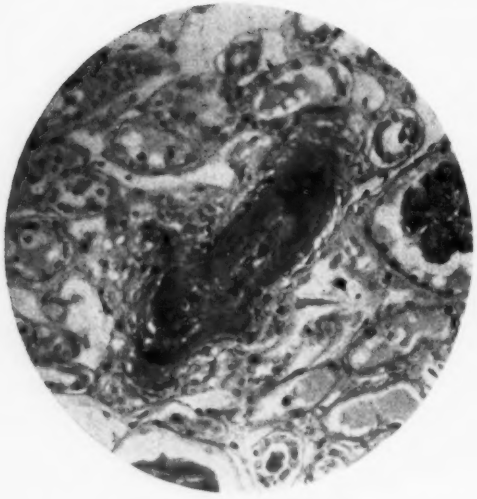

Fig. 11.

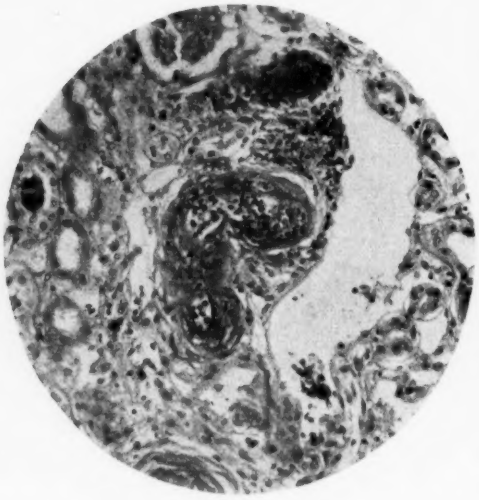

Fig. 12.

Fig. 11. A small lobular arteriole, almost completely replaced by a tube of coagulated plasma and fibrin. The lumen is very narrow, the endothelial cells are swollen. There is beginning organization by a proliferation of adventitial cells. (Hæmatoxylin and eosin.) ×170.

Fig. 12. Small lobular artery showing a severe and fresh lesion. The layers of the walls are split apart and saturated with plasma, red blood cells, and polymorphonuclear leucocytes. There are red blood cells and polymorphonuclear leucocytes within the lumen. (Hæmatoxylin and eosin.) ×170.

Fig. 13. Afferent arteriole and glomerulus. The lumen of the afferent arteriole is distended with blood, the subendothelial basement membrane is fragmented and the wall is saturated with blood. There is an aneurismal dilatation of the afferent vessel just after entering the glomerulus. There is a hæmorrhage into the vessel wall and into the framework of the glomerular tuft. Some of the capillaries of the glomerulus are collapsed; others show extreme dilatation with fragmentation of the basement membrane and hæmorrhage into the capsular space and proximal convoluted tubule. The overlying epithelial cells are swollen, granular, and some contain hæmosiderin. (Hæmatoxylin and eosin.) ×121.

Fig. 14. Afferent arteriole and glomerulus. Both are unusually large. The wall of the arteriole is saturated with plasma. The lumen is partially occluded with a fibrin thrombus. The same changes are seen in portions of the glomerular tuft in which blood cells, plasma, and fibrin appear beneath the endothelium of the capillaries, often obstructing the lumen. The overlying epithelial cells, and cells of the capsule show degeneration and desquamation. There are scattered polymorphonuclear leucocytes and red blood cells, together with fibrin and precipitated protein within the capsular space. (Hæmatoxylin and eosin.) ×121.

Fig. 15. Two glomeruli with their respective afferent arterioles. The walls of the afferent arterioles are saturated with plasma, fibrin, and fragmented red blood cells. Their lumina are partially thrombosed. In the one glomerulus the capillary tuft is collapsed; in the other the capillaries are overdistended with blood, the basement membrane is stretched, and there are red blood cells within the capsular space and convoluted tubules. (Hæmatoxylin and eosin.) ×115.

Fig. 16. Glomerulus showing aneurismal dilatation of the afferent vessel after entering the glomerulus. The lumen of this vessel is distended with red blood cells and the wall is saturated with blood and fibrin. Many of the capillaries contain red blood cells; others are collapsed. The walls of the capillaries are thickened by a reduplication of the basement membrane and also by an increase in the ground substance beneath the endothelium. (Hæmatoxylin and eosin.) ×170.

died a clinically nephritic death following a chronic nephritic toxæmia of pregnancy.

On the other hand, Volhard and Fahr (1914) and Fahr (1934) called attention to a condition which was characterized by marked elevation of blood pressure, and a quickly fatal course with uræmic death. This appeared in individuals of middle life and about equally in males and females. The histological findings in the small arteries and arterioles throughout the body were characterized by necrotizing changes of the wall, saturation of the walls with plasma and red blood cells, and proliferation of the endothelium and connective tissue of the intima described as an endarteritis which often led to apparent occlusion of the lumen. These were found scattered throughout the body but particularly in the kidney and also in the pancreas, adrenal, gastrointestinal tract, and brain. The changes in

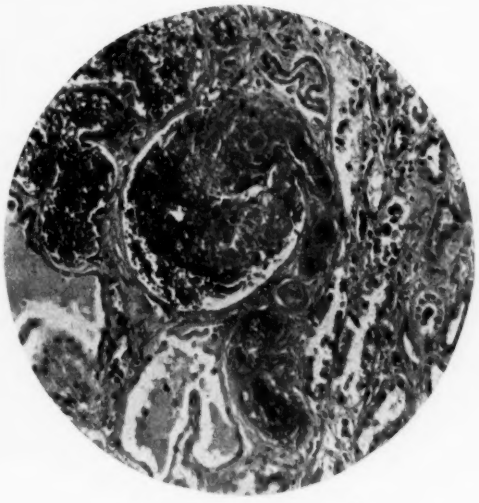

Fig. 13.

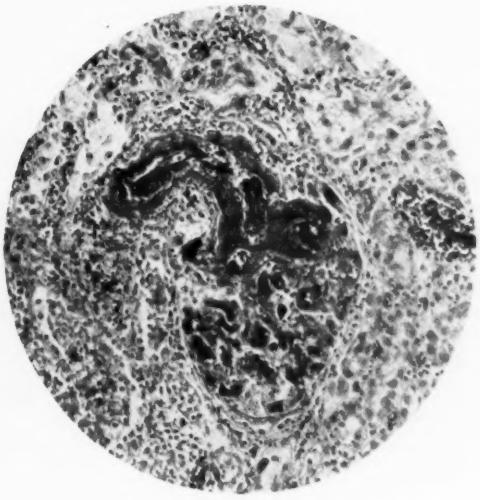

Fig. 14.

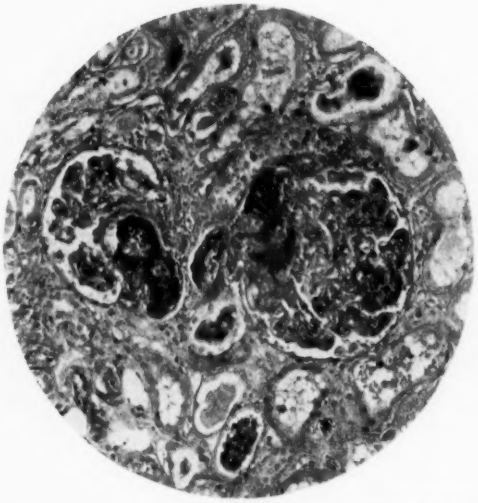

Fig. 15.

(Legend on opposite page.)

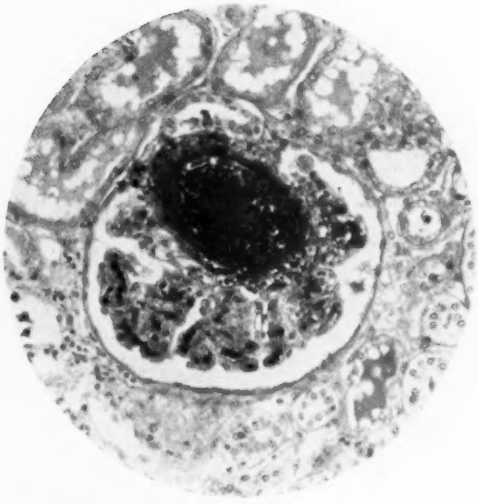

Fig. 16.

the kidney involved not only the large and smaller vessels, but also the glomeruli and tubules. Unlike the lesions of diffuse glomerulonephritis which are found in all glomeruli, the changes here tend to be focal, involving single or groups of glomeruli in a degenerative and inflammatory process. The tubules present a picture in which the changes in the lining epithelium vary from slight degeneration to necrosis and desquamation. This they described as a pathological entity under the term malignant nephrosclerosis. This work was confirmed and extended by Schuermann and MacMahon (1933) and others. Much work has been carried on in studying this condition, but the etiological relation of the toxæmias of pregnancy has not as yet been described.

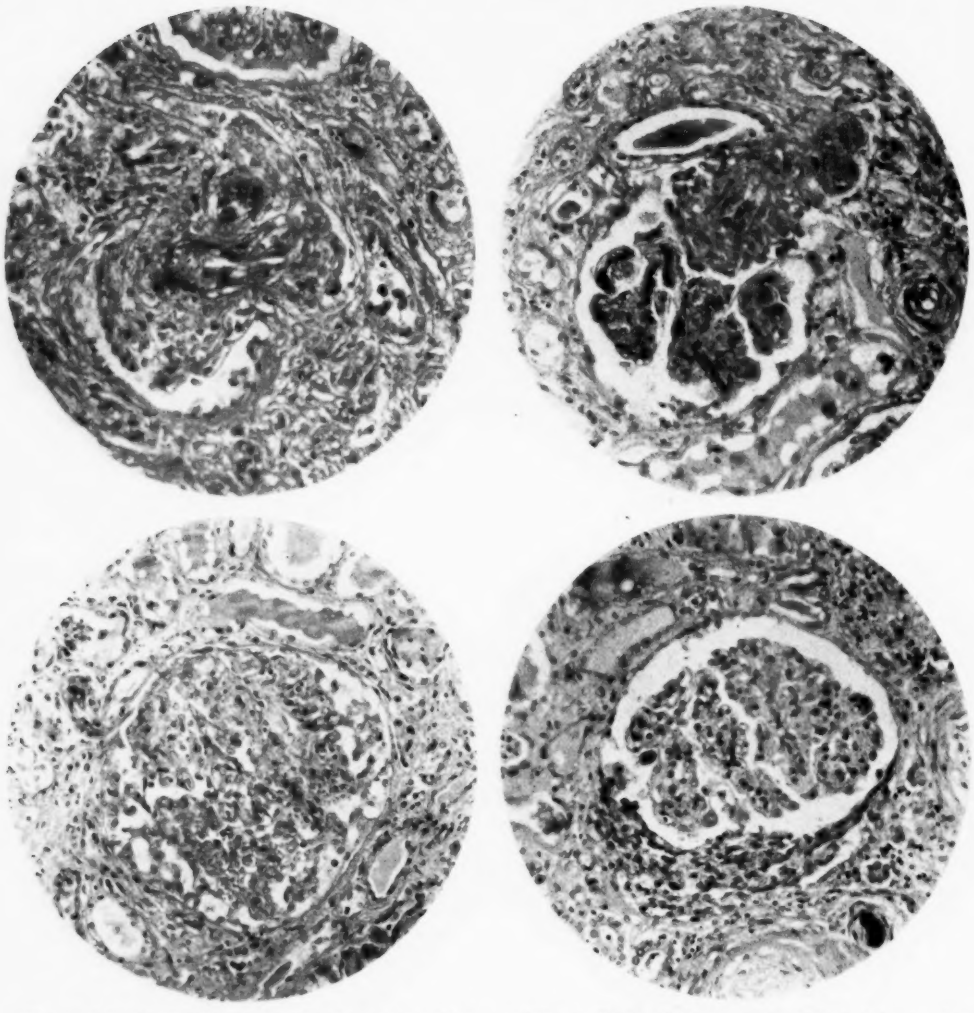

Fig. 17, left, above. Glomerulus, showing an organizing process with proliferation of endothelial cells which form a tongue-like projection growing into the dilated afferent arteriole, partially occluding the lumen. There are still residual fibrin and fragmented red blood cells within the structure of the glomerulus. The proliferating endothelial cells are separated by a newly formed delicate intercellular fibrillar reticulum. The basement membrane of the capsule is absent along one side and swollen and fibrillated along the other. (Hæmatoxylin and eosin.) ×165.

Fig. 18, right, above. Glomerulus, showing a still later stage than Figure 17. At the pole of the glomerulus, proliferating endothelial cells together with their intercellular fibrillar reticulum have formed a small granuloma-like nodule. This represents a late stage in the organization and repair of the injured afferent vessel as seen in Figure 16. The lumen of the afferent arteriole is not completely occluded, and the capillaries of the glomerular tuft contain a moderate amount of blood. (Hæmatoxylin and eosin.) ×170.

Fig. 19, left below. Glomerulus, greatly enlarged. Most striking is the proliferation of the epithelial cells covering the capillary tuft and capsule; they form adhesions between the tuft and the capsule and often build small gland-like structures. The capillaries of this glomerulus contain a small amount of blood and there is an increase in ground substance and scattered hæmorrhages into the capillary walls. (Hæmatoxylin and eosin.) ×125.

Fig. 20, right, below. Glomerulus. Most striking is the well developed crescent of proliferating capsular epithelial cells. The capillaries of the glomerulus contain little blood. The walls of the capillaries are thickened by an increase in subendothelial ground substance. The epithelial cells covering the capillaries are large and show droplet degeneration. (Hæmatoxylin and eosin.) ×155.

DESCRIPTION OF CASES

CASE 1. J.H.H.U. 34614 T-534. Patient aged 40 years, colored, 4 full term pregnancies,1 living child Weight 174¼ pounds.

The patient was seen at age 33 years, at which time she was 7½ months pregnant. The blood pressure was 190/100, the urine contained 0.8 gram albumin (Esbach). She was admitted for study but left the hospital against advice and was delivered elsewhere of a stillborn fetus. At age of 35 years she returned in labor with a blood pressure of 250/130 and delivered spontaneously.

At age of 40 years, she returned, not pregnant, complaining of "pain in the stomach, swelling of the legs, and difficulty in getting the breath." Patient stated that her father had died of "bladder trouble" and her mother of "kidney trouble." Her blood pressure was 148/96, eyegrounds showed "marked vascular retinitis, bilateral." The phenolsulphonphthalein test showed less than 5 per cent excretion in first and second hour. The non-protein nitrogen of the blood was 208 milligrams per cent and the uric acid 9.8 milligrams per cent. The urine contained one plus albumen, 1 to 3 white blood cells per high power field and no red blood cells. The blood pressure rose after admission to 262/160 millimeters mercury and the patient died. Clinical diagnosis: chronic nephritis with terminal uræmia.

Autopsy showed "generalized arteriolosclerosis; arteriolosclerotic nephritis; necrosis in the pancreas; cardiac hypertrophy and fatty heart; chronic passive congestion of the lungs and lobular pneumonia."

Microscopic examination of kidney. The normal architecture of the kidney is almost completely lost. The cortex and medulla are poorly demarcated and the surface is finely granular. There is a chronic process involving the vessels, glomeruli, and tubules which has led to considerable and diffuse sclerosis of the cortex. Superimposed on this is an acute, destructive lesion of the vessels and glomeruli with hæmorrhage throughout the walls of the small vessels, and capillary dilatation within the glomeruli. There are, in places, extensive hæmorrhages into the capsular spaces. These histological changes constitute a classical example of well advanced malignant nephrosclerosis. A description of the finer details of this case will serve as a standard for the others of its class to be described.

Vessels. The entire arterial tree shows marked hypertrophy of the vessel wall (Fig. 1). In the interlobar, arcuate, and larger branches of the lobular arteries, the media is thickened and well preserved. There is a connective tissue thickening of the adventitia and of the intima. In the latter is seen a well developed lamellar elastosis (Fig. 2).

The smaller lobular arteries and the afferent vessels to the glomeruli show replacement of their muscular media by connective tissue. Three important changes in the intima are also seen. The most common is the endarteritis obliterans in which the thickened intima appears as concentric rings of cells and intercellular substance which frequently produces an apparent occlusion of the lumen (Figs. 4, 5, 6, 7, 8, 9). Another lesion is the presence of a variable quantity of a poorly differentiated ground substance beneath the endothelium (Fig. 10). Finally, and most striking, there are fresh hæmorrhages throughout the vessel walls (Figs. 11, 12).

Glomeruli. More than 90 per cent of the glomeruli are still moderately well preserved. They are larger than normal, slightly more cellular, decidedly anæmic and show an increase in the basement membrane and subendothelial ground substance. Superimposed on these changes are the fresh lesions so characteristic in the glomeruli of malignant nephrosclerosis. There are aneurismal dilatation of the capillaries, rupture of the basement membrane, and extensive hæmorrhages into the capsular space and tubules (Figs. 13, 14, 15, 16). In glomeruli in which this lesion is somewhat older are seen proliferation of both endothelial and epithelial cells (Figs. 17, 18, 19, 20), and in still older lesions, an organizing process with sclerosis and adhesions between the tuft and the capsule.

A few scattered glomeruli are acellular and show hyaline transformation. The epithelial cells covering the glomerular tufts are frequently seen to be swollen with hyaline droplet degeneration.

Tubules. The changes in the tubules are much more marked than those in the glomeruli. Those still recognizable as well differentiated proximal convoluted tubules are only occasionally seen and then usually in small islands at the periphery of the cortex. The great majority of the tubules are small, atrophic, and collapsed. Many have disappeared entirely. The epithelial cells lining the tubules show degenerative changes and desquamation. Within the lumina are red blood cells, polymorphonuclear leucocytes, cellular débris, and precipitated protein.

Stroma. There is a diffuse increase in the connective tissue stroma which occasionally shows a focal lymphocytic infiltration.

Adrenal and pancreas. The changes in both large and small vessels of the adrenal and pancreas are similar to those already described in the kidney, although the lesions are less striking. The pancreas shows, in addition, areas of pancreatic necrosis.

The most striking changes in the kidney are those of the vascular tree. There is the vascular hypertrophy, the intimal elastosis, the proliferating endarteritis, and the hæmorrhage and necrosis of the walls. The tubules show widespread atrophy and disappearance, and present a striking contrast to the large number of fairly well preserved glomeruli. The latter show the increase in size and anæmia so commonly seen in malignant nephrosclerosis, also the acute lesions—hæmorrhage into the tuft and the walls of the capillaries of the tuft, and into the capsular space. These lesions are characteristic of malignant nephrosclerosis.

CASE 2. J.H.H.U. 30132 T-542. Patient aged 24 years, colored, has had 1 pregnancy at term, 1 abortion, 1 living child. At age of 17 years she had a soft chancre. Physical examination at that time revealed no other abnormality. Wassermann was negative. At age of 21 years she was admitted at 8½ to 9 months pregnant. Her mother died of "jaundice"; her father of "heart trouble." Blood pressure was 220/140. Urine showed an occasional granular cast, albumin, a faint trace and many white blood cells. Blood non-protein nitrogen was normal. Uric acid was 5.1 milligram per cent. Eyegrounds showed "retinal œdema." The blood pressure fell quickly after delivery and at discharge was 118/90.

At age of 22 years, patient returned 4½ to 5 months pregnant. Blood pressure was 220/130. Urine was negative for albumin. Eyegrounds showed "retinal œdema." Urea clearance was 74 per cent. On observation with bed rest the blood pressure fell to 124/88 and patient was discharged. She was readmitted one month later. Blood pressure was then 170/120, eyegrounds were normal, the urine negative. Hysterotomy and tubal sterilization were done. Six weeks after operation, blood pressure was 160/100, urine negative.

Six months after operation, patient was readmitted for study. Blood pressure on admission 193/155, fell to 160/105 on discharge. Examination showed blood chemistry and urine normal. Eyegrounds showed "retinal œdema."

One year after operation, blood pressure was 255/180 and the patient complained of "dizzy spells." Interval blood pressures were about of this level.

The patient was readmitted at age of 24 years, complaining of headaches, dyspnœa, and blurring of vision. Blood pressure was 270/180; urine, albumin faint trace; eyegrounds, "renal retinitis and arteriolosclerosis." Phenolsulphonphthalein test 2 hour excretion, was 35 per cent; Mosenthal test, fixed specific gravity; urine, occasional red blood cell and white blood cell.

She was discharged but readmitted shortly thereafter with a blood pressure of 240/160, complaining of dyspnœa and showing evidence of cardiac decompensation. Eyegrounds showed retinal hæmorrhages. Urine contained many white blood cells, occasional red blood cells and casts. The patient died on the fourth day. Clinical diagnosis: chronic cardiovascular-renal disease.

Autopsy report was not available.

Microscopic examination of kidney. Here, too, the architecture of the cortex is greatly altered as a result of the atrophy and disappearance of the tubules in some areas and their dilatation and elongation in others. The vessels show the same lesions as in Case 1, but these are more frequently seen and more severe. One of the striking features is that the few remaining well differentiated proximal convoluted tubules are localized in areas at the very periphery of the cortex and resemble, in this regard, the zones of healthy tissue seen in Case 5.

Vessels. The lesions in the vascular tree are as described in the standard Case 1. Hæmorrhage and saturation with plasma of the walls of the smaller vessels is commonly seen (Figs. 11, 12). In the lobular arteries, these fresh lesions are largely limited to the intima and the elastic lamina appears stretched but unbroken. These changes may frequently be traced to the corresponding glomerulus which shows in turn a similar change (Figs. 13, 14, 15, 16). There are older lesions in which the fibrin in the wall of the small vessels shows organization, and granuloma-like formations are seen along the afferent arterioles (Figs. 17, 18). The endothelium of these small vessels is swollen and shows proliferation. Fibrin thrombi occasionally obstruct the lumina.

Glomeruli. The glomerular lesions are typical of those seen in malignant nephrosclerosis. The proportion of glomeruli in a state of reasonable preservation to those which have been destroyed and have become hyaline is as in Case 1. The same changes in the relatively intact glomeruli are seen. In some of the afferent arterioles there is seen what appears to be a very recent aneurismal dilatation where the vessel enters the glomerulus (Fig. 16). There is hæmorrhage into the walls of these vessels and into the capsular space while the capillaries of the tuft are dilated (Figs. 13, 14, 15).

Tubules and stroma. These show the same changes as those described in Case 1.

Pancreas and adrenal. The arterioles of both organs show hypertrophy of the media. The small vessels show hyaline transformation of their walls. The arterioles of the pancreas show, in addition, plasma beneath the endothelium although this is not frequently found.

The lesions in this case are similar in every respect to those described in the standard case. The histological findings suggest that the process has been the most severe of the group.

CASE 3. J.H.H.U. 18867 T-535. Patient aged 36 years, colored, has had 5 term pregnancies, 3 abortions, 5 living children. At age of 31 years she was observed throughout a pregnancy. The systolic blood pressure reached 158 millimeters mercury and the diastolic 106 millimeters mercury. The urine was negative throughout. The weight 151 pounds. At age of 32 years she was observed during another pregnancy. Highest systolic blood pressure was 150 millimeters mercury, highest diastolic 112 millimeters mercury. Urine was negative throughout. The weight reached 167 pounds. At the age of 34 years she again became pregnant and was admitted at the sixth month. Blood pressure was 214/170, urine contained two plus albumin; weight was 170 pounds. After admission the blood pressure rose to 236/174. Phenolsulphonphthalein test showed 22 per cent in first hour, 13 per cent second hour. "Marked retinal arteriosclerosis and arteriosclerotic retinitis." There was œdema of the extremities, urine contained albumin 2–3 plus, fine granular casts and red blood cells.

The patient aborted spontaneously. She was seen a year later, not pregnant, blood pressure 210/150; urine, albumin 2 plus. One year after this a blood pressure of 224/170 was recorded.

At age of 36 she again became pregnant and was admitted at 3 to 4 months. Blood pressure 200/140. Phenolsulphonphthalein test, 35 per cent excreted in first hour, 20 per cent second hour. Blood non-protein nitrogen was normal. Urine showed albumin 3 plus with fine granular casts and red blood cells. The patient was sterilized by hysterectomy. Six weeks later, blood pressure was 200/150; urine, albumin 1 plus. Four weeks later, blood pressure was 210/170.

Eight months *post abortum* the patient was admitted, not pregnant, complaining of "headaches and bloody urine." Blood pressure was 258/198, phenolsulphonphthalein test, 8 per cent in 2 hours. Non-protein nitrogen of blood 85.6 milligrams per cent. The 24 hour urine volume varied between 400 and 600 cubic centimeters. The patient died. Clinical diagnosis: chronic nephritis.

Autopsy showed "chronic arteriolosclerotic nephritis; cardiac hypertrophy with myocardial scarring; lobular pneumonia; slight perivascular mononuclear infiltration in the medulla; slight arteriosclerosis of aorta; adenomata of thyroid; hypophyseal duct cyst with atrophic changes in the hypophysis."

Microscopic examination of kidney. The kidney architecture is moderately well preserved although there is a diffuse increase in the connective tissue throughout the cortex and fine granulation of the surface. The vessel changes are characteristic of malignant nephrosclerosis.

Vessels. Lesions are similar in all respects to the standard Case 1.

Glomeruli. Most glomeruli are fairly well preserved. The most striking lesions are the recent degenerative and inflammatory changes. These present an accumulation of ground substance between the endothelium and the basement membrane producing apparent complete occlusion of the lumen of the capillaries. In these glomeruli the endothelial cells are increased in number and the overlying epithelial cells show marked swelling, droplet degeneration, and proliferation. These cells are found continuous with those of the capsular wall (Fig. 19). There are no aneurismal dilatations although occasionally red blood cells are found within the capsular space.

Tubules and stroma. The lesions here are as described in Case 1, although in this case a greater number of tubules retain their differentiation.

Pancreas. There is hypertrophy of the media of the larger arteries; sclerosis and hæmorrhage into the wall are seen in the smaller arterioles. In general the lesions are similar to those seen in the vessels of the kidney although of lesser degree.

Again the most striking lesion is that of the arterial tree of the kidney. The changes in the glomeruli and tubules are not far advanced and are largely degenerative. The changes are typical of those described in malignant nephrosclerosis, although the lesions in this case are not so advanced as in Cases 1 and 2.

CASE 4. J.H.H.U. 29163 T-539. Patient aged 37 years, colored, had had 4 pregnancies at term, 2 abortions, 4 living children. Her weight was 119 pounds. At age of 35 years, not pregnant, blood pressure was 288/140. Wassermann was negative. Family history was negative. At age of 36 years she was admitted to hospital 5 months pregnant. Blood pressure was 230/160; moderate cardiac hypertrophy; no abnormal symptoms. "Eyegrounds normal save for attenuation of arteries." Phenolsulphonphthalein test showed 15 per cent first hour, 25 per cent second hour. Urine revealed a trace of albumin; otherwise negative. Therapeutic abortion and sterilization were done. On discharge, blood pressure was 160/115; urine, negative.

The patient was observed frequently following this. The blood pressure continued at about the level of 230/150 and the urine remained negative. She complained of occasional headaches.

At age of 37 years she was admitted, not pregnant. Blood pressure was 240/150. Eyegrounds showed "moderate arteriolosclerosis without hæmorrhages or exudates." Blood non-protein nitrogen was 57.8 milligrams per cent. Blood uric acid 7.2 milligrams per cent. Urea clearance test 7.5 per cent. Urine showed occasional white blood cells and granular casts, albumin 3.5 grams (Esbach). The patient died. Clinical diagnosis: chronic nephritis.

Autopsy showed "chronic nephritis with hæmorrhages; cardiac hypertrophy; subendocardial hæmorrhages; fat in myocardium; cystitis; . . . lobular pneumonia."

Microscopic examination of kidney. The lesions in the component parts of the kidney are very similar to those in Case 3. The lesions are typical of those described as malignant nephrosclerosis but the severity of the lesions in this case is the least of those described in this series.

The vessels present the same picture as that in the standard Case 1. Fewer glomeruli are anæmic and fewer have undergone hyaline degeneration. There is no marked capsular change, and adhesions are rare. The majority of the tubules are still well differentiated although granular and droplet degeneration are common.

The striking lesion, again, is in the arterial tree of the kidney and both chronic and fresh lesions may be recognized. The tubules in general are moderately well preserved. Only kidney tissue was available for study.

Two cases showed variations from those described as typical of malignant nephrosclerosis. The first of these, Case 5, shows an exaggeration of the usual lesions with an added

infarction of the cortex. It presents the most severe form of the lesions seen in this series. A description of this case is followed by that of Case 6 which may be placed at the opposite end of the list. It represents a transitional stage between malignant nephrosclerosis and the lesions of what has been described as benign nephrosclerosis. The histological findings are similar to those of malignant nephrosclerosis but are of a mild degree in comparison with the typical picture as described above.

CASE 5. J.H.H.U. 791 T-533. Patient aged 35 years, colored, had had 8 full term pregnancies, 7 premature labors, 1 abortion, 6 living children. There are available records of 4 previous pregnancies. At the age of 20 and 26, two pregnancies were normal. At 28 years, a pregnancy was complicated by a blood pressure of 130 millimeters mercury as highest systolic and 95 millimeters mercury as highest diastolic. There was a moderately severe pyelitis of short duration, but the pregnancy went to term and ended spontaneously. At 29 years, there was another term pregnancy with highest systolic blood pressure of 145 millimeters mercury and highest diastolic of 95 millimeters mercury. The urine was negative throughout. The Wassermann was also negative. The patient said that her mother had died of "dropsy."

The present pregnancy ended in the spontaneous abortion of a 5 to 6 month fetus elsewhere. The patient had suffered throughout pregnancy from "dim vision and a sense of weakness." Interference with vision became more marked postpartum and the patient was admitted. The findings on admission were: blood pressure 186/140, temperature 98.6 degrees F.; urine, albumin 4 plus, specific gravity 1.012, no casts or red blood cells. External ocular muscle movements were poorly performed. The following day the patient showed twitching of the right arm and leg. The blood pressure had risen to 202/144, hæmoglobin 38 per cent, and there was a leucocytosis of 20,720. Phenolsulphonphthalein test showed no excretion in either the first or second hour and the non-protein nitrogen of the blood was 162.5 milligrams per cent. On successive days the non-protein nitrogen of the blood rose to 240 and 285 milligrams per cent. The Wassermann reaction was negative. The patient died. Clinical diagnosis: chronic nephritis with uræmia.

Autopsy showed "puerperal uterus with infection; chronic diffuse nephritis with necrosis and thrombosis of the arterioles; infarctions of the kidney; multiple necroses of the pancreas; hyperplastic bone marrow; alteration of the spleen; œdema of the lungs with slight lobular pneumonia."

Microscopic examination of kidney. The normal architecture of the kidney is greatly distorted. The cortex and medulla are not sharply demarcated and the cortex lacks an orderly arrangement. The surface is pitted. There are two outstanding lesions. The first and more spectacular is the presence of recent scattered infarcts in the cortex. The other is a more chronic process with sclerosis of the medium sized and small vessels, apparent obliteration of the lumina of these vessels, and widespread atrophy of the cortex with streaks of fibrosis of its stroma. These areas of fibrosis frequently present a triangular outline with the base at the peripheral portion of the cortex. As a result of these lesions there is very little well preserved cortical parenchyma.

Vessels. The interlobar, arcuate, and lobular arteries are all of unusually large diameter. The media in the larger of these is not only thickened but well preserved. The adventitia and intima are also thickened with reduplication of the internal elastic lamina of the latter. In spite of this increase in the thickness of the walls of the larger arteries the lumina are still larger than those of the corresponding vessels of the normal kidney.

The changes in the smaller vessels are similar to those described in the typical cases of malignant nephrosclerosis. Similar changes are seen even in some of the larger lobular arteries (Fig. 3). Fibrin thrombi are frequently seen and the replacement of the muscular media by connective tissue is marked. The smaller vessels are unusually tortuous. The saturation of the vessel walls is also exaggerated in degree and frequency. Plasma may be seen in all layers, and red blood cells and occasional polymorphonuclear leucocytes are found within the walls and may even be traced into the surrounding stroma. This is often associated with thrombosis of the lumen of the vessel.

Glomeruli. The glomerular changes are similar to those described with the typical cases except that they tend here to be obscured by the presence of fresh areas of ischæmic necrosis.

Tubules. These also present the changes described as typical, with the additional factor as in the glomeruli. Many are filled with red blood cells, broken-down, desquamated cells and hyaline and granular casts.

Stroma. The older lesions are characterized by an increase in connective tissue and an infiltration with lymphocytes. The fresh lesions show œdema and hæmorrhage.

Veins and capillaries. The intertubular capillaries and veins are moderately distended but no histological change can be recognized.

Basement membrane. Due to the marked increase in subendothelial ground substance and the secondary organization, the basement membrane of the small arteriole is often difficult to trace. Occasionally it appears to be interrupted and bathed in plasma. In the glomerular tuft it is often wrinkled, thickened, and reduplicated.

Adrenal. The small arteries in the capsule show only hypertrophy of the media whereas in the small arterioles in the medullary portion there is hyaline swelling of the basement membrane without necrotizing arteriolitis such as is seen in the kidney.

The lesions seen here are an exaggeration of those described in the typical case. The chief lesion is that of the arterial tree in the kidney. The vascular hypertrophy, arteriolosclerosis, and arteriolonecrosis are characteristic of malignant nephrosclerosis. This necrosis is so extensive and so frequently associated with thrombosis that it is not surprising to find many areas of ischæmic necrosis of the cortex. There is, then, a chronic process involving the vessels, glomeruli, and tubules. Superimposed upon this, is recent vascular damage with necrosis of the vessel walls, thrombosis, and infarct formation.

This case is similar to a group described by Von Zalka (1932–1933) under the term "symmetrical cortical necrosis of the kidney." His cases were more advanced and the necrosis more widely spread. They showed either a massive necrosis or multiple infarcts of the cortex but never with involvement of the medulla. He described hyalinization of the lobular arteries, afferent arterioles, and glomeruli with fibrinous thrombi in the lumina. In his own case he speaks specifically of vascular necrosis. Altogether, the condition which he describes has a marked resemblance to that in the present case, although in his opinion he was not dealing with malignant nephrosclerosis.

What is equally important from the point of view of the present discussion is that he recognized the relation of "cortical necrosis" to pregnancy. He states that of 37 cases collected from the literature, 31 were possibly related to pregnancy. Three, however, occurred in males and three more were not related to pregnancy. This is the closest approach to a recognition of the relation between the vascular changes described in this paper and the toxæmias of pregnancy which a search of the literature has brought to light.

CASE 6. J.H.H.U. 8662 T-531. Patient aged 29 years, colored, 6 previous pregnancies, 1 abortion, and 2 living children. The first child was stillborn. The second and third are alive and well. The last three pregnancies produced stillborn children and in the last of these pregnancies the patient is said to have had convulsions. When first seen there was a pregnancy of 2½ to 3 months' duration. The heart was enlarged to clinical examination, the blood pressure 208 millimeters mercury systolic and 110 millimeters mercury diastolic. The weight was 218 pounds. The urine contained a moderate amount of albumin. The patient was admitted 2 days later when the blood pressure was found to be 256/140, the urine contained albumin, occasional leucocytes, and some cellular casts. Specific gravity was 1.011. Mosenthal test showed a fixation of specific gravity of 0.010 but a varied quantity and a large night volume. Blood non-protein nitrogen was 42.8 milligrams per cent. A hysterectomy was done. Three days after operation, the non-protein nitrogen of the blood had risen to 120 milligrams per cent, and some granular casts and some red blood cells appeared in the urine. The patient died on the eighth day after operation. Clinical diagnosis: peritonitis; chronic nephritis with uræmia.

Autopsy showed "suppuration of the abdominal incision, purulent pelvic peritonitis, early generalized peritonitis, chronic nephritis and moderate arteriosclerosis. . . ."

Microscopic examination of kidney. There is considerable change from the normal architecture of the cortex, with some reconstruction. The surface is irregular and there is moderate scarring in the form of irregularly interlacing paths of connective tissue. The most striking lesion is seen within the arterial tree. This shows a vascular hypertrophy and a sclerosis of the small arterioles. The interlobar, the arcuate, and the first portions of the lobular arteries show a dilatation of their lumina, a thickening of the muscular media and, here and there, a reduplication of the internal elastic lamina. The distant portions of the lobular arteries and the afferent arterioles to the glomeruli show in contrast a rather striking group of changes. These vessels are tortuous, the muscular media is replaced by connective tissue, and the subendothelial ground substance is increased to such an extent as to cause in places apparent complete occlusion of the lumen. Less commonly, small granuloma-like formations are seen along the vessels where they approach the glomeruli.

Most of the glomeruli are moderately increased in size and show a slight increase in the number of cells. The basement membrane itself is unchanged but the overlying epithelial cells are swollen and show hyaline droplet degeneration. The epithelium lining the capsule is also swollen and the cytoplasm shows similar regressive changes. The basement membrane of the capsule is unchanged. A relatively small number of glomeruli, in large measure confined to the areas of cortical scarring, are small, contracted and acellular and show complete hyaline transformation. Occasional adhesions between the glomerular tuft and the capsule are seen.

There remain a moderate number of easily recognizable tubules appearing usually in the form of islands bordered by tracts of scar tissue. The lumina are dilated and contain little precipitated protein. The lining epithelial cells are cuboidal with indistinct cell boundaries. The cytoplasm shows both granular and droplet degeneration. The basement membrane is unchanged. In contrast to these are

the changes seen in the tubules in the areas of sclerosis. These are small, collapsed, and their narrowed lumina contain minute hyaline casts. The basement membrane of these is thickened, wrinkled, reduplicated, and there is occasionally an acellular ground substance between these double layers of basement membrane. In the lumina of some of the collecting tubules are granular deposits of hæmoglobin.

In the areas of tubular atrophy there is an increase in connective tissue. This is infiltrated with lymphocytes and frequently shows well developed lymphoid tissue in which reticulum is clearly recognizable.

Pancreas and adrenal. The large and small arteries of the adrenal and pancreas show much the same changes as those described in the kidney. There are hypertrophy of the media of the larger vessels and intimal sclerosis with occlusion of the smaller arteries. The larger vessels show enlargement of their transverse diameter. The smaller show hyaline degeneration of the entire wall but neither necrosis nor hæmorrhage. The lesions here may be described as those of arteriolosclerosis.

The type of the vascular change is characteristic of neither benign nephrosclerosis with its hyaline swelling of the basement membrane nor of malignant nephrosclerosis with its interruption of the basement membrane and saturation of the wall with blood and plasma. It apparently represents a transitional stage. The tracts of sclerosis within the cortex correspond to the distribution of the more severe vascular lesions. The degenerative changes in the epithelium of the glomeruli and tubules are apparently recent and may be considered as a mild glomerulo-tubulo-nephrosis. This is in contrast to the older vascular lesions. The patient died with peritonitis, presumably before the lesions of malignant nephrosclerosis had had time for complete development.

These cases have a number of features in common. The condition occurs in relatively young women, usually between 30 and 40 years of age. All have become pregnant in the presence of hypertensive disease which has been adversely affected by the pregnancy. In many, the original hypertensive disease appeared during the course of a toxæmia of pregnancy. After a varying period of time during which hypertension was the only feature common to all, there was a sudden appearance of other symptoms referable to both the cardiovascular and urinary systems and the patients quickly thereafter died. Death in all cases was shown to be associated with uræmia. Pregnancy occurring in the presence of a hypertension or of a chronic nephritis following a pregnancy toxæmia seems to play an important rôle in the production of the acute lesions of malignant nephrosclerosis. The degree of the interval hypertension, and its duration are also determining factors. It must be stressed that all of these had had a hypertension of some duration. As will be seen later none of the cases in which death occurred during a toxæmia with hypertension for the first time showed the vascular lesions within the kidney of malignant nephrosclerosis, although in patients dying with eclampsia, vascular lesions may be found within the liver identical with the acute lesions of malignant nephrosclerosis.

The microscopical examination shows the most striking lesions to be in the vascular system. These are best seen in the kidney but may also be recognized in the vessels of other organs. They show clearly a chronic condition manifested by hypertrophy of the larger and smaller arteries of the vascular bed. There is an hypertrophy of the muscular media and thickening of the adventitia. The total diameter of an artery and that of the lumen is greatly enlarged. Superimposed upon this are other lesions in the small arteries and arterioles and in the glomeruli tubules and stroma. These are characterized by:

1. Thickening and hypertrophy of the intima of the arterioles with frequent apparent occlusion of the lumina (Figs. 4, 5, 6, 7, 8, 9, 10).

2. Saturation of the wall of the smaller vessels with blood plasma and red blood cells (Figs. 11, 12).

3. Damage to scattered groups of glomeruli. These changes include aneurismal dilatation of the walls of the afferent arterioles after they have entered the glomerulus, saturation of their walls with plasma and red blood cells, and hæmorrhage into the glomerular capsule and proximal portions of the tubules. The finer histological changes have been described above (Figs. 13, 14, 15, 16).

4. Destruction of the tubules and increase in the connective tissue stroma of the cortex. Small islands of dilated tubules remain at the periphery of the cortex.

These are the lesions described as those of malignant nephrosclerosis. It is significant that every patient who fell into this clinical group showed the same histological picture. The question naturally arises as to whether or not all patients who have residual damage in the form of obstetrical chronic nephritis following a pregnancy toxæmia and who later die with clinical symptoms of uræmia will show the same clinical and histological picture. This cannot be answered by the present study. It should be pointed out, however, that the cases described above, together with those which follow, make up all of the material which it was possible to obtain from the obstetrical service records of Johns Hopkins Hospital. The chance of sampling error is inherent in the study of such small groups, but no other element of choice has interfered.

A further group of 5 cases died with a clinical diagnosis of nephritis. It will be seen at once that these differ from the malignant nephrosclerosis group since in none of them is there a history of hypertension before the present pregnancy.

CASE 7. J.H.H.U. 13203 T-540. Patient was 27 years of age, white, and had had 2 term pregnancies with no living children. At 23 years of age a pregnancy was observed during which blood pressures of 110/86 and 122/92 were recorded. On admission at term, the urine contained albumin 2 plus and a few hyaline casts.

At 27 years of age, patient was seen when 3 to 4 months pregnant. Blood pressure was 148/100. The urine showed a trace of albumin. She was admitted for study. The eyegrounds showed "moderate retinal œdema, moderate arteriosclerosis." Urea clearance was 86 per cent. Highest blood pressure was 162/115. Blood chemistry analysis revealed normal findings. The blood pressure fell and she was discharged. The blood Wassermann was positive but we have no record of treatment. She was readmitted 2 months later complaining of "dizziness." The blood pressure ranged about 150/100; the urine was negative; the weight 194½–199 pounds. There developed œdema, generalized and in the lungs, dyspnœa and orthopnœa. The patient died, undelivered, 2 months after admission, with a diagnosis of chronic nephritis, arteriosclerosis, and cardiac decompensation.

Autopsy report showed: "heart hypertrophied with hypertrophic musculature and old scars; arterioles reveal hyaline changes in kidney and pancreas; intracapillary and glomerular changes in the kidney; lungs, chronic passive congestion; liver, slight catarrhal atrophy; cells beneath capsule of liver and in lung capillaries which closely resemble chorionic cells; liver, patchy areas of dilated sinusoids surround areas in which the liver cell capillaries show what appear to be fibrin thrombi. It resembles the liver of eclampsia but the lesions are mid-zonal."

Microscopic examination of kidney. The normal architecture of the kidney is well preserved. The one striking pathological finding is a degenerative change in the epithelium of the glomerulus and tubules. These cells are remarkably swollen and granular. The lumina are almost obliterated, although precipitated albumin and hæmoglobin casts may be seen. The vessels and stroma show no pathological change.

Pancreas and adrenal. The vessels in these organs show no lesions.

The findings here are those of glomerulo-tubulo-nephrosis and the histological lesions are similar to those of the eclamptic nephrosis.

CASE 8. J.H.H.U. 40316 T-536. This woman aged 33 years, colored, had had 4 term pregnancies, 4 living children. All of these were delivered elsewhere and there were no available observations until the patient was admitted about 8 months pregnant, complaining of swelling of the hands and feet and blurring of vision of 3 weeks' duration. Blood pressure was 230/160. Urine, albumin 1.5 grams (Esbach), showed numerous red blood cells, white blood cells, and occasional fine granular casts. The eyegrounds showed "advanced renal retinitis with moderate arteriolosclerotic changes and some neuroretinitis." Blood non-protein nitrogen was 41 milligrams per cent. Blood uric acid was 8 milligrams per cent. A cæsarean section was done. Blood non-protein nitrogen rose to 57.8 milligrams per cent and uric acid to 11.4 milligrams per cent. The patient died on the second day after operation. Clinical diagnosis: chronic nephritis.

Autopsy showed "flabby kidneys containing much fat; old scars and cyst in right kidney; dilated right ureter containing pus; hæmorrhage in adrenal; myocardial hypertrophy; hæmorrhages beneath the endocardium. . . ."

Microscopic examination of kidney. The normal architecture is well preserved. There is marked swelling of the tubular epithelium with granulation of its cytoplasm. The glomerular capillaries contain blood. The epithelium covering the tuft is slightly swollen. The vessels and stroma are unchanged.

Pancreas and adrenal. Both large and small vessels show no pathological findings.

The histological diagnosis is acute tubular nephrosis without vascular change.

CASE 9. J.H.H.U. 12058 T-543. This woman, aged 39 years, white, had had 4 term pregnancies, 1 abortion, 4 living children. All pregnancies were observed elsewhere. When first seen the patient

was at term, blood pressure 220/140. Urinalysis showed albumin 4 grams (Esbach). She was admitted at once and labor induced by means of a bag. Delivery was accomplished by version and extraction under chloroform anæsthesia and was followed by a postpartum hæmorrhage of 1200 cubic centimeters with some evidence of shock. The patient died on the same day. Clinical diagnosis: pre-eclamptic toxæmia, postpartum hæmorrhage and shock.

Autopsy showed "history of manual delivery, hæmorrhage and shock; postpartum uterus containing blood clot; bilateral tears of the lower uterine segment and cervix; chronic nephritis; petechial hæmorrhages of heart and skin of lower extremities; old mitral endocarditis; focal necrosis of liver. . . ."

Microscopic examination of kidney. The normal architecture is well preserved. The important pathological lesion is degeneration of the tubules with swelling of the epithelium and narrowing of the lumen. In an occasional tubule the cells show necrosis and calcification. The glomeruli show little change and the vessels and stroma show none.

Pancreas and adrenal. These show little change although there is enough hyaline transformation of the arteriolar walls of the pancreas to allow a diagnosis of slight arteriolosclerosis.

The changes here are those of a tubular nephrosis in the acute stage. The arteriolosclerosis in the pancreas is so slight as to be negligible.

CASE 10. J.H.H.U. 7288 T-538. This patient, aged 15 years, colored, had had no previous pregnancies. She was admitted 7 months pregnant. There was a history of occasional hæmoptysis. A right sided pyelitis was found with pyuria. The urine contained staphylococci but no tubercle bacilli. Temperature remained normal throughout. The urine contained many white blood cells, a few red blood cells, and albumin 2 plus. No blood pressure readings were taken. Spontaneous labor yielded a stillborn premature fetus. The placenta was diagnosed as syphilitic. The patient died. Clinical details are lacking.

An autopsy report on this patient was not available.

Microscopic examination of kidney. The normal architecture of the kidney is slightly distorted through an irregularity in the arrangement of the tubules. These show degeneration but also regeneration in areas where cells have been destroyed. Within the lumina of the tubules may be seen red blood cells, polymorphonuclear leucocytes, fibrin and precipitated protein, with scattered desquamated epithelial cells. The surrounding stroma in these areas of regeneration is slightly increased and œdematous and shows a fairly rich infiltration with inflammatory cells. Neither vessels nor glomeruli show significant changes.

Pancreas and adrenal. The arteries and arterioles show no pathological changes.

This case shows the characteristics of a tubular nephritis. There are no vascular changes.

CASE 11. J.H.H.U. 5911 T-541. Patient aged 40 years, had had 2 abortions. When first seen, she was 8 months pregnant. The urine contained 2 grams of albumin (Esbach), specific gravity 1.018–1.020, moderate number of granular casts. Hæmoglobin was 42 per cent. Blood pressure was 170 millimeters mercury systolic. A placenta prævia was diagnosed and delivery by cæsarean section at term, under chloroform anæsthesia, was carried out. The patient died on the sixth day after operation. Clinical details are lacking.

Autopsy showed "acute endometritis; acute diphtheritic colitis; hæmoperitoneum; fatty degeneration of the liver; chronic diffuse nephritis; chronic adhesive pleurisy; perihepatitis and perisplenitis. . . ."

Microscopic examination of kidney. The normal architecture of the kidney is preserved. There is granular degeneration of the epithelium of the tubules. They are dilated and contain large quantities of precipitated protein and casts. The glomeruli show some swelling of the epithelium. There is muscular hypertrophy of the vessels which is most marked in the larger stems. The stroma is essentially unchanged although there are minute foci of sclerosis and of lymphocytic infiltration.

Pancreas and adrenal. The arteries and arterioles show no pathological changes.

This, Case 11, is a tubular nephrosis with vascular hypertrophy.

Cases 7, 8, 9, 10, and 11 represent the clinical and pathological picture of toxæmias of pregnancy occurring for what is presumed to be the first time. They all show the lesions characteristic of that condition. What is more important from the point of view of this study is that none shows the lesions of malignant nephrosclerosis. Case 11 and to a much lesser degree, Case 9, with vascular hypertrophy, might be considered as potential malignant nephrosclerotics in whom the time interval and the degree of damage were not yet sufficient for the development of the typical lesions.

For the sake of completeness two further cases are given brief description.

CASE 12. J.H.H.U. 6320 T-537. Patient, colored, aged 32 years, had had no pregnancies. She had typhoid at age of 18. At age of 28 years, not pregnant, blood pressure was 174/130. At age of 29 years, not pregnant, blood pressure was 134/88. At age of 32 she was first seen when 6½ months pregnant. Blood pressure was 190/120 and 170/110. Urine was negative for albumin. Four days later, blood pres-

sure was 150/110. Eyegrounds were normal. Phenolsulphonphthalein test showed 55 per cent excretion first hour, 10 per cent second hour. Patient complained of vomiting. Sixteen days later, she was still vomiting and blood pressure was 130/86. The pulse rose to 140–150, and blood pressure of 140/108 was recorded. Patient aborted a 9 months' stillborn fetus. Throughout this time the blood non-protein nitrogen was normal. The patient died. Clinical diagnosis: chronic nephritic toxæmia.

Autopsy report was not available but a note was made by an observer from the obstetrical service to the effect that the "right kidney showed marked destruction of the substance with multiple abscesses; no dilatation of pelvis of right kidney; left kidney showed many hæmorrhagic areas and a few abscesses; few patches of broncho-pneumonia."

Microscopic examination. The kidney showed typical lesions of malignant nephrosclerosis. No abscesses were present. The vessels of the pancreas showed only hypertrophy of the media. The adrenal showed hypertrophy of the arteries of the capsule with marked arteriolosclerosis and hæmorrhage into the walls.

The lesions here are typical of malignant nephrosclerosis. The original damage was not associated with pregnancy since death occurred following the first of these. The pregnancy was, however, implanted upon a preexisting hypertension.

This case is not included in the consideration of the group of malignant nephrosclerosis for the reason that the observation of abscesses in the kidney was reported and none was found on microscopic examination. That it belongs in the group is reasonable to suppose but the uncertainty of identity has demanded a separate report.

CASE 13. J.H.H.U. 36650 T-532. This woman, aged 39 years, colored, had had 5 term pregnancies, 4 living children. At age of 13 years a term pregnancy was observed. The urine at one time contained ¼ gram albumin (Esbach). No further data. At age of 25 years, term pregnancy, no data. At age of 26 years, term pregnancy, blood pressure and urine normal.

At age of 29 years, term pregnancy, two blood pressures of 135/90 and 140/100 were recorded. Urine albumin trace, once.

At age of 39 years, patient was admitted pregnant and close to term. She had complained of vomiting and headaches for 2 weeks. Two hours before admission she became comatose. Her mother had died of "apoplexy." Eyegrounds, "retinal œdema, bilateral." Blood pressure was 105/80. Urine showed albumin 4 plus, large numbers of red blood cells and white blood cells. Blood non-protein nitrogen 193.5 milligrams per cent. Blood uric acid was 14.5 milligrams per cent. Hæmoglobin was 16 per cent, white blood cells 15,000, red blood cells 920,000. A cæsarean section with hysterectomy was done. The patient died 4 days later of septicæmia complications, chronic nephritic toxæmia of pregnancy.

Autopsy showed "chronic cystitis and pyelonephritis; organizing and fresh thrombi in the pelvic veins; multiple small emboli in lungs; confluent lobular pneumonia; acute splenic tumor; swollen liver with hydropic cells; hyperplasia of the bone marrow; multiple infected thrombi in the hypophysis with extensive necroses; embolus in right middle cerebral artery; foci of fresh encephalomalacia with bacteria; local myocarditis; scars in myocardium; cholelithiasis; focal scars in liver."

Microscopic examination of kidney. Well preserved kidney showing moderate vascular hypertrophy. Superimposed upon this is a fresh degenerative and inflammatory reaction involving the tubules, glomeruli, and stroma. Some of the capillaries of the glomeruli are filled with organisms. The tubules show granular and fatty degeneration of the cytoplasm of the epithelium. The stroma is œdematous and contains polymorphonuclear leucocytes and lymphocytic exudate.

Pancreas. Vessels show no pathological change. There is a diffuse interstitial pancreatitis.

This patient died with septicæmia. As a result of this there is bacterial focal glomerulonephritis and simple tubular nephrosis with toxic œdema of the stroma. There is also a mild simple arteriolosclerosis with vascular hypertrophy which played no part in the fatal issue. Lesions of malignant nephrosclerosis are not present.

SUMMARY

1. The toxæmias of pregnancy frequently produce permanent vascular damage to the patient. Many of these women die in a short period of time. Statistical evidence of this from the literature is presented.

2. A clinical and histological study of all of the deaths indexed as from nephritis which have occurred on the obstetrical service of Johns Hopkins Hospital and from which pathological material was available is reported.

3. Two groups of cases have emerged: (a) Those in which the patient died during or immediately following a pregnancy complicated by a non-convulsive toxæmia and in whom no history of previous hypertension was obtained, showed tubulonephrosis and in no case, the characteristic lesions described as malignant nephrosclerosis.

(b) The second group is made up of those patients who have suffered from a chronic nephritic toxæmia of pregnancy. In every case the hypertension has preceded the last pregnancy and has existed for from 2 to 7 years before death. Every patient in this group was found to present the characteristic lesions of malignant nephrosclerosis as described by Volhard and Fahr (1914) and Fahr (1934).

We wish to take this opportunity to express our appreciation to Professor W. G. MacCallum of the Department of Pathology, Johns Hopkins Hospital, for permission to use the material here presented.

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THE RECURRENT LARYNGEAL NERVES IN TOTAL ABLATION OF THE NORMAL THYROID GLAND

An Anatomical and Surgical Study[1]

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THE recurrent laryngeal nerves constitute the greatest technical hazard in total ablation of the normal thyroid gland. This procedure for the treatment of angina pectoris and congestive heart failure was recently advanced by Blumgart and his co-workers at the Beth Israel Hospital in Boston(5). Of a total number of more than 70 complete thyroidectomies, 65 were performed for the relief of advanced cardiac disease, and the encouraging results thus far achieved augur well for its useful application in angina pectoris and other forms of chronic heart disease. The operative technique and results have been reported elsewhere (2, 6).

The purpose of this communication is to call attention to the technical hazard of the recurrent nerve, pointing out its various vulnerable juxtapositions to the gland and thus to assist the surgeon in avoiding serious nerve injury, with its consequent disastrous vocal cord complications. The extensive operation of removing the entire thyroid gland obviously presents a great risk of injury to the recurrent nerves. An accurate knowledge of the variations in the relationship of these nerves to the thyroid gland then is of vital assistance to the operator in the prevention of abductor paralysis. It is this variability of position, rather than the vulnerability of the nerve itself that is responsible for the frequency with which it may be seriously injured.

ANATOMICAL DISSECTIONS OF THE RECURRENTS IN SEVENTY CADAVERS

During the past 2 years anatomical dissections were made of both recurrent laryngeal nerves in 70 cadavers. Particular study was made of the position of the nerve in relation to the thyroid gland and its adherent zone (Fig. 3b). In a previous communication (2) the latter area was described as an expression of normal anatomy indicating the fixation of the gland to the trachea just below the anterolateral aspect of the bar of the cricoid cartilage at the level of the first and second tracheal rings. The anatomical courses of the nerves were conveniently classified into three groups (Table I).

Group I. The most hazardous position of the nerve in relation to the gland is shown in Figures 3c, 4a, 4b, and 5. Ten per cent, or 14, of a total of 140 nerves, were found partially penetrating the gland, 9 on the right side, 5 on the left. When encountered in this vulnerable position, the nerve is carefully dislodged by blunt dissection from its surrounding bed of glandular tissue.

Group II. Approximately 25 per cent of the nerves were demonstrated traversing the adherent zone (Fig. 3b and 3d), 19 on the right and 16 on the left side. After mobilization of the corresponding lobe by the ligation and severance of the lateral thyroid vein and the vessels of the upper and lower poles, the adherent zone is brought into view. Subsequent traction on the lobe reveals the pronounced fixation of the gland to the trachea at this point. Frequently, the nerve is concealed in this region beneath a stratum of fibrofascial and fatty tissue. By careful exploration with a blunt instrument it is possible to identify and preserve the nerve uninjured.

Group III. In our dissections, 65 per cent of the nerves were found coursing safely in the tracheo-œsophageal sulcus, in which position the nerve is best protected against operative injury (Figs. 3a, 6a, and 6b). The classical anatomical textbooks in their description refer only to this position of the nerve, not mentioning either the possibility of partial penetration of the gland by the nerve or the important relationship existing between the nerve and the adherent zone.

[1] This is the twelfth study of the treatment of chronic heart disease by producing a subnormal metabolic rate in patients with no evidence of thyrotoxicosis.

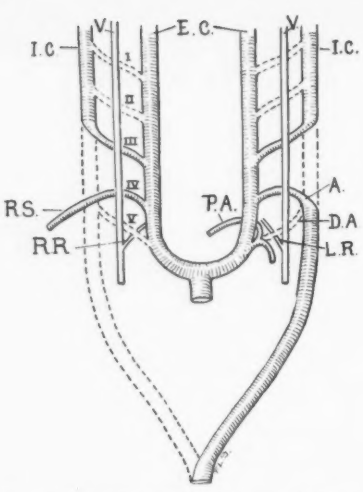


Fig. 1. Aortic arches of the embryo. (After Minot.) The dotted lines represent those vessels which normally disappear. *A*, Aorta; *E. C.*, external carotid artery; *I. C.*, internal carotid artery; *P. A.*, pulmonary artery; *R. S.*, right subclavian artery; *D. A.*, ductus arteriosus; *V.*, vagus nerve; *L. R.*, left recurrent laryngeal nerve; *R. R.*, right recurrent laryngeal nerve.

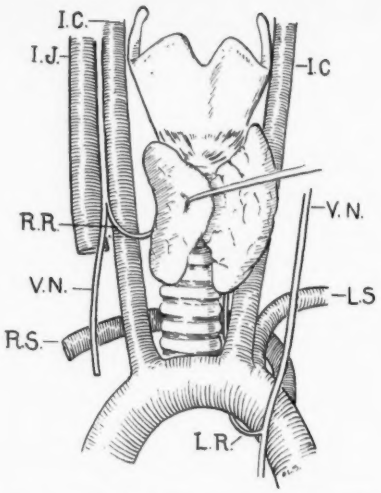


Fig. 2. Diagram of the common associated anomalies of the right recurrent laryngeal nerve and aortic arch. The right subclavian artery is shown arising as the last branch of the aortic arch and passing behind the trachea and œsophagus toward the right arm. *R. R.*, Right recurrent nerve; *V. N.*, vagus nerve; *L. R.*, left recurrent nerve; *I. J.*, internal jugular vein; *I. C.*, internal carotid artery; *R. S.*, right subclavian artery; *L. S.*, left subclavian artery.

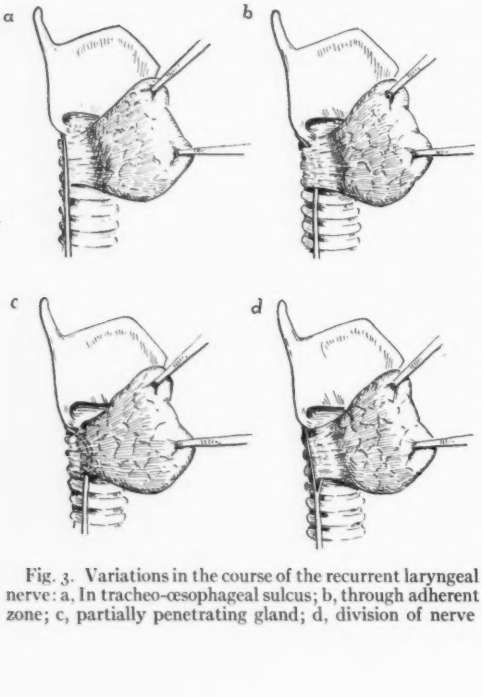


Fig. 3. Variations in the course of the recurrent laryngeal nerve: a, In tracheo-œsophageal sulcus; b, through adherent zone; c, partially penetrating gland; d, division of nerve

COMPARATIVE SURGICAL OBSERVATIONS OF THE RECURRENT LARYNGEAL NERVE IN SEVENTY TOTAL ABLATIONS OF THE NORMAL THYROID

Observations were made in a total number of 72 recurrent nerves in the course of 70 total thyroidectomies. Table II demonstrates the different positions occupied by the nerve as demonstrated at the operating table. For the sake of comparison, they are classified in a manner similar to those demonstrated in the anatomical laboratory (Table I). The percentages are calculated on the basis of the possible total of 140 nerves.

Group I. Nine nerves (7 per cent) were demonstrated partially penetrating the gland. To release the recurrent nerve from this, its most vulnerable position, meticulous and deliberate dissection is required to avoid injury.

Group II. Forty-five nerves (32 per cent), 24 on the right and 21 on the left side, were identified coursing through the adherent zone in a very intimate position to the gland, necessitating careful blunt dissection for the intact preservation of the nerve.

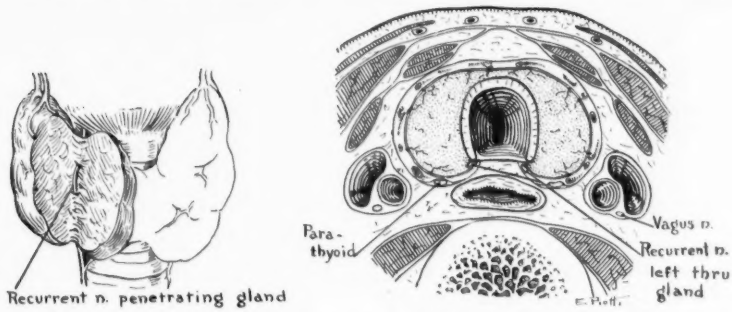


Fig. 4. Anteroposterior and cross section views showing partial penetration of the thyroid gland by the recurrent laryngeal nerve. Anteroposterior view and cross section demonstrating left nerve through the gland (after Gorning).

Group III. Eighteen nerves were identified in the tracheo-œsophageal sulcus. Sixty-eight nerves were not identified at operation. Presumably, they were safely concealed deep in the tracheo-œsophageal sulcus. When the thyroid was found deeply molded in the groove between the trachea and œsophagus, presenting either a retrotracheal or retrolaryngeal prolongation, it was necessary to expose the course of the nerve in the sulcus to assure its protection. Fowler and Hanson found 5 glands in 200 (2½ per cent) extending retrotracheally. In our operative series 4 glands (5.7 per cent) presented either retrotracheal or retrolaryngeal prolongations.

TABLE I.—CLASSIFICATION OF VARIOUS POSITIONS OF THE RECURRENT LARYNGEAL NERVES (ANATOMICAL DISSECTIONS OF BOTH NERVES IN 70 CADAVERS)

	Right	Left	Total Per cent
1. Partially penetrating gland	9	5	10
2. Through adherent zone	19	16	25
3. In tracheo-œsophageal sulcus	42	49	65
	70	70	100

TABLE II.—CLASSIFICATION OF VARIOUS POSITIONS OF THE RECURRENT LARYNGEAL NERVES (SURGICAL OBSERVATIONS IN 70 TOTAL THYROIDECTOMIES)

	Right	Left	Total Per cent
1. Partially penetrating gland	5	4	7
2. Through adherent zone	23	20	31
a. Branching before entering larynx	1	1	1
3. In tracheo-œsophageal sulcus	8	10	13
4. Unidentified*	33	35	48
	70	70	100

*Presumably these nerves coursed beyond reach deeply in the tracheo-œsophageal sulcus.

RELATIONS OF THE RECURRENT NERVE TO THE TRACHEA AND INFERIOR THYROID ARTERY

An observation made in the anatomical laboratory which has a practical surgical application, concerns the relationship of the recurrent nerve to the lateral surface of the trachea. On the left side the nerve ascends in a vertical plane and is intimately applied to the trachea along its entire course in the neck. On the right side at the base of the neck, the nerve is frequently separated from the trachea to the average extent of about 1 centimeter, gradually approximating the trachea in its upward ascent and becoming closely apposed to the latter upon reaching the adherent zone. At the level of the lower pole the right nerve is often found thus separated from the trachea and, in addition, usually travels in

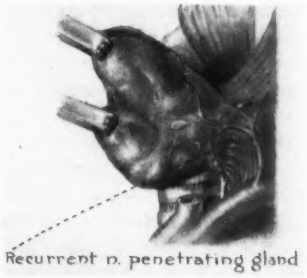


Fig. 5. Recurrent nerve partially penetrating gland.

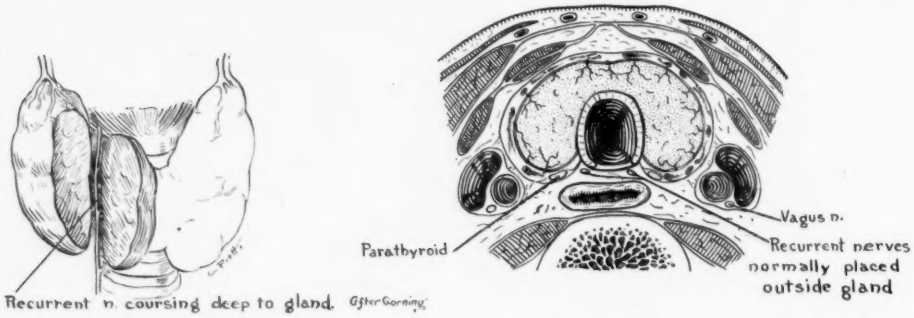


Fig. 6. Anteroposterior and cross section views demonstrating the recurrent laryngeal nerves coursing in the tracheo-œsophageal sulcus deep to the gland.

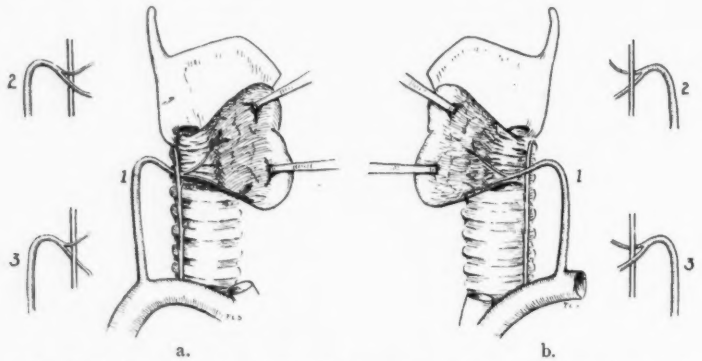
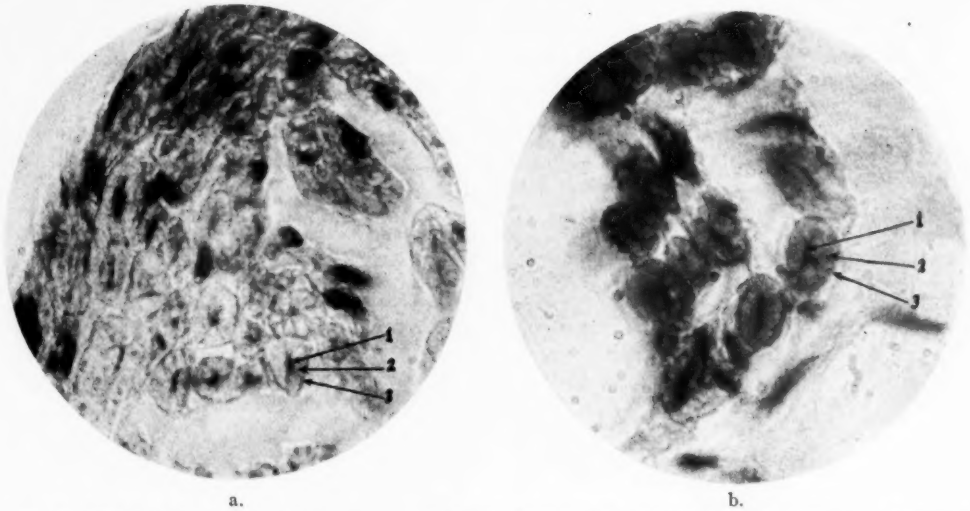


Fig. 7. Variations in the relationship between the nerve and inferior thyroid artery. a, Right side: *1*, nerve anterior to artery; *2*, nerve posterior to artery; *3*, nerve passing between terminal branches. b, Left side; *1*, nerve anterior to artery; *2*, nerve posterior to artery; *3*, nerve passing between terminal branches.

a more anterior plane than its fellow opposite. This vulnerable combination of anatomical relationships has been often observed at operation. If not recognized the nerve may easily be caught in a snap or accidentally cut.

The cartilaginous prominence of the inferior thyrocricoid articulation affords an especially valuable surgical landmark for identifying the location of the recurrent laryngeal nerve as it enters the cavity of the larynx, for each of the 140 nerves dissected was seen to pass posteriorly to this articulation. Ziegelman, in a dissection of 42 recurrent nerves, also observed that all of the nerves presented a similar relationship to the inferior cornua of the thyroid cartilage on both sides. It should be again emphasized, however, that the nerve may arch anteriorly, traversing the adherent zone or partially penetrating the gland, before dipping beneath the cornu (Figs. 3b, 3c, 4a, and 5). Fortunately, in the majority of instances (65 per cent) the nerve ascends vertically in the tracheo-œsophageal groove on both sides, beyond harm's reach.

Twice the nerve was demonstrated branching into two terminal twigs at about the level of the lower pole, the anterior branch coursing through the adherent zone and ultimately joining its posterior terminal companion beneath the inferior thyrocricoid joint (Fig. 3d). One such reasonably sizeable anterior branch was accidentally cut at operation on the left side after first identifying the posterior twig which was thought to be the main stem of the nerve, with a resultant partial temporary paralysis of the corresponding vocal cord.



a. b.

Fig. 8. Histological resemblance between recurrent laryngeal nerve and an ordinary peripheral nerve: a, Recurrent laryngeal nerve. High power showing nerve fibers with, *1*, axis cylinders, *2*, myelin sheath, and, *3*, neurolemma. ×925. b, Subscapular nerve. High power showing nerve fibers with, *1*, axis cylinders; *2*, myelin sheath; and, *3*, neurolemma. ×925.

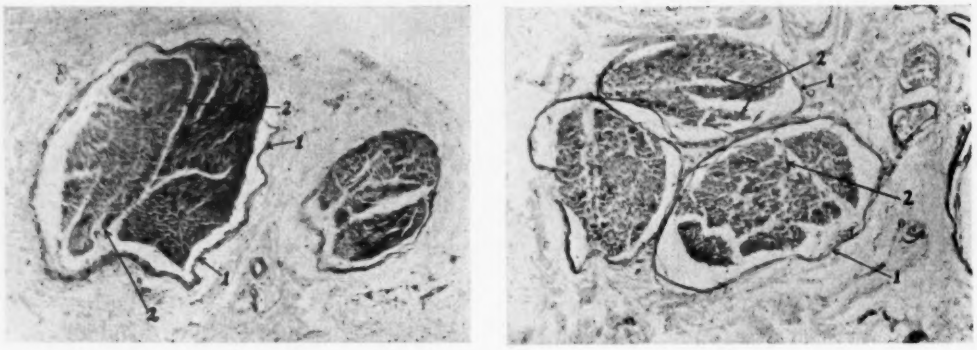
In a previous publication (4) the results of 22 neck dissections disclosed, in a comparison of both sides, a marked discrepancy in the relationship existing between the recurrent nerve and inferior thyroid artery. It was pointed out that the nerve was much more often anterior to the artery on the right side than on the left side. In this present series a reasonable but not so pronounced difference between the two sides was observed in the relationships of these structures (Figs. 7a and 7b).

	Left	Per Cent	Right	Per Cent
Posterior to artery.....	44	63	31	44
Anterior to artery.....	17	24	28	40
Between terminal branches	9	13	11	16
	70		70	

It is obvious from this table that the nerve may frequently be anterior to the artery on either side, and the surgeon must be constantly on the alert to recognize such variations when invading the danger zone in the final steps of total ablation of the thyroid gland.

EMBRYOLOGY AND ANOMALIES OF THE RECURRENT LARYNGEAL NERVE

Accidental injury to the nerve is most likely to occur when its position is anomalous. Fortunately, however, anomalies of the recurrent laryngeal nerve are rare. The only type which has been encountered in the literature is an anomalous course of the right recurrent nerve, which seems to occur in about 1 of every 500 persons. It appears to be more frequent in negroes (1). In the cases described, the nerve becomes separated from the main trunk of the vagus at about the level of the cricothyroid articulation. It may then run on in the carotid sheath for as much as 5 centimeters before passing medialward to the tracheo-œsophageal sulcus, up which it runs to a normal distribution as the inferior laryngeal nerve (1, 3, 10, 13, 14). In some instances the nerve may not actually exist as such, being replaced by several smaller filaments (1, 13). This anomaly has regularly been observed in association with an abnormal aortic arch; the right subclavian artery, instead of coming from the innominate of that side, arising either as the last branch of the aortic arch or from the dorsal aorta itself. In those cases to the reports of which we have had access, the subclavian artery passed behind the trachea and œsophagus to the right arm (1, 14).



a. b.

Fig. 9. a, Recurrent laryngeal nerve. Low power showing two fasciculi, *1*, perineurium, and, *2*, endoneurium. ×75. b, Subscapular nerve. Low power showing five fasciculi, *1*, perineurium, and, *2*, endoneurium. ×75.

This association of anomalies is easily explained on an embryological basis. In Figure 1 (12), it will be seen that in the young embryo the inferior laryngeal nerves leave the vagus in the neck and pass medially and dorsally under the fifth aortic arch to the site of the larynx. In the normal course of events as the heart and the great vessels descend into the thorax, the left nerve is dragged down by the ductus arteriosus, which eventually comes to lie in the vertical plane, so that the nerve *appears* to hook around the aorta. The right nerve, on the other hand, is pulled down by the fourth arch, which later becomes the subclavian artery. If the fourth aortic arch on the right side fails to develop, and the subclavian artery of that side comes directly off the aorta, the right recurrent nerve has only the internal carotid artery above it. This, in man, is almost vertical in position, and naturally does not pull the nerve down to any great extent, so that the latter goes almost directly across the neck from vagus to larynx (Fig. 2).

One would expect that in persons with right-sided aortas, any anomaly of the recurrent nerve would be on the left side. To our knowledge no such case has appeared in the literature, but the findings in one that was seen in the Harvard anatomical laboratory last winter were very kindly furnished by Dr. Weatherford of that school. There was a right sided aorta, from the dorsal portion of which the left subclavian artery sprang, to pass behind the trachea and œsophagus on its way to the left arm. On the right, the recurrent nerve looped around the aorta, as would be expected. On the left, however, the nerve left the vagus at the level of the subclavian artery, looped around a strand of fibrous tissue in *front* of the vessel, and ascended the neck in the tracheo-œsophageal sulcus as usual. To explain this anomaly, we must assume that the fibrous tissue about which the nerve hooked represents the sclerosed remnant of either the fourth or fifth left aortic arch.

VULNERABILITY OF THE RECURRENT LARYNGEAL NERVE

Crile contends that the slightest direct or even indirect pressure on the nerve will interfere with its conduction and immediately change the voice. We have not observed this extreme sensitivity of the nerve to such slight trauma. While the possible inclusion of the recurrent nerve in a ligature is viewed with considerable fear, its vulnerability, because of certain characteristics in its conductivity (7), is not as great as has been supposed. This was our experience in 43 patients in whom one or both nerves were demonstrated at operation and subjected to manipulative insult such as would ordinarily attend this type of a dissection. There were 8 temporary vocal cord paralyses. Knowing that in some instances paresis followed the inadvertent pinching of the nerves, it seems probable that trauma of this character was responsible for the pareses

in these instances. There were three permanent unilateral cord paralyses. One of these was proved at post mortem to result from ligation; another resulted from accidental section of the nerve. In no instance did permanent bilateral vocal cord paralysis develop.

The foregoing clinical observations are in accord with the animal experimental findings of Judd, New, and Mann, who demonstrated that, while stretching will not result in any impairment of nerve function, pinching will cause temporary paralysis of the corresponding cord, and that permanent cord paralysis will follow ligation or severance of the nerve.

The recurrent laryngeal nerve has been designated as being soft and naked, in contrast with a peripheral nerve (7). Histologically, there does not appear to be a valid basis for this differentiation (Figs. 8a, 8b, 9a, and 9b). Both the recurrents and the peripheral nerves are furnished with a myelin sheath and a neurolemma (sheath of Schwann). A naked nerve is considered to be one devoid of these coverings. Furthermore, the perineurium or connective tissue element in the recurrent laryngeal nerve is essentially as abundant as in the average peripheral nerve; hence its firmness and tensile strength should be comparable to those of a peripheral nerve.

THE IMPORTANCE OF LARYNGOSCOPIC EXAMINATION IN THE COURSE OF OPERATION

Laryngoscopic examination preceding each operation should be a routine procedure in the management of all thyroid surgery, in order to assure pre-operative normality of the vocal cords and to enable one to ascertain more accurately the postoperative incidence of recurrent nerve damage. Injury to both recurrent laryngeal nerves is a calamitous, but fortunately an uncommon complication of subtotal resection of the diseased thyroid gland. There is greater likelihood, however, of such a tragic accident developing in the process of totally extirpating the gland; for, whereas in the customary subtotal thyroidectomy the danger zone of the recurrent nerves and the parathyroid glandules is not particularly disturbed, in total thyroidectomy this zone is deliberately invaded (2). Thus, in the latter operation both nerves are exposed to the greatest possible harm, and the danger of bilateral nerve injury must be always regarded as imminent. As a precaution against the development of such a complication, a direct laryngoscopic examination of the vocal cords is made routinely after the removal of one lobe (9). This applies to cases in which operation has been done under local, as well as general anæsthesia, for on occasion the voice may be apparently normal even in the presence of one-sided nerve injury. The quality of the spoken voice, therefore, is not a reliable guide to the integrity of the recurrent nerve on the corresponding side operated upon. Such false reliance on the changes in the character of the voice may lead to serious consequences. In the face of vocal cord paralysis after extirpation of one lobe, operation is ended to avoid the possibility of bilateral nerve injury. In two patients this procedure was followed with subsequent return of function of the injured recurrent nerve, and successful removal of all remaining thyroid tissue at a second operation.

Recently, at the suggestion of Dr. L. M. Freedman, we have desensitized the throats of patients operated upon under local anæsthesia by applying cocaine immediately preceding operation, in order to alleviate the discomfort of direct laryngoscopic examination during operation.

SUMMARY

1. Attention is called to the increased danger of injury to the recurrent laryngeal nerve in total ablation of the thyroid gland over that present in partial thyroidectomy.

2. The recognized type of gross anomaly in the course of the nerve is described and an embryological explanation for it is offered.

3. A report of the dissections of 140 recurrent nerves in 70 cadavers is presented. The nerves are classified into three groups as they are found in the tracheo-œsophageal sulcus, traversing the adherent zone, or partially penetrating the thyroid gland itself. The incidence of the latter two positions is found to be sufficiently great to demand the concern of the surgeon constantly. Operative experience confirms these observations.

4. The importance of the inferior thyrocricoid articulation as a guide to the location of the recurrent laryngeal nerve is strongly emphasized.

5. Although the nerve is found to be anterior to the inferior thyroid artery more often on the right than on the left, the disproportion is not extremely marked, and this position of the nerve should be watched for on both sides of the neck.

6. Clinical and histological evidence is presented to show that the recurrent laryngeal nerve closely resembles an ordinary peripheral nerve and that its vulnerability to trauma is not as great as previously supposed. It is felt that an accurate knowledge of the variable positions of the nerves is the essential factor in the prevention of bilateral injury to the nerve.

7. The quality of the spoken voice cannot be relied upon to denote the presence of unilateral nerve damage. The necessity, therefore, for direct laryngoscopic examination after ablating one lobe of the thyroid as a prevention against bilateral vocal cord paralysis is again emphasized.

I desire to express my appreciation to Dr. Charles G. Mixter, surgeon-in-chief of the Beth Israel Hospital, for his encouragement throughout this work.

I am indebted to Dr. Monroe J. Schlesinger, pathologist to the Beth Israel Hospital, for the preparation of histological material.

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ALTERATIONS IN LIVER GLYCOGEN FOLLOWING THYROID, IODINE, AND GLUCOSE FEEDINGS

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OF the numerous conditions in clinical practice in which a serious depletion of the liver glycogen may play an important part, none is more frequently encountered than is hyperthyroidism. Although the exact relation of thyroid function to the regulation of carbohydrate metabolism is as yet a moot point, there is sufficient available evidence published by different investigators—Cramer and Krause, Boesl, Zimmerman, and Knittel—to state that the feeding of desiccated thyroid extract to the cat, rat, mouse, guinea pig, or rabbit results in a reduction of the liver glycogen.

While certain of these investigations may be criticized because of failure more adequately to control the conditions surrounding the experiments, the data may be accepted as a whole, as there is no essential disagreement between them.

We were primarily interested in whether or not the liver glycogen would be increased in the presence of experimental hyperthyroidism by the addition of glucose to the normal diet. During these investigations, we have also had the opportunity to obtain additional evidence on the effect of the iodides on the circulating thyroxin.

METHOD

The animals used in these experiments were guinea pigs from one stock. They weighed from 400 to 600 grams. Purina rabbit pellets, which contain approximately 16.5 per cent of protein, 4 per cent of fat, 52.8 per cent of nitrogen free extract and 7.8 per cent of fiber, were used for feeding. The pellets were pulverized and remolded into squares containing approximately 16 grams.

When thyroid extract, potassium iodide or glucose was added to the diet, it was mixed with the pellets during the process of pulverizing.

The pigs were weighed daily at the same time before feeding. Special feedings were as a rule not begun until each group had been observed carefully for at least 1 week and the animals had shown a normal weight increase during this period. In the special feeding experiments, only data from those animals which ate all the food given them are included.

After a variable period of feeding, the pig was stunned by a cranial blow, the abdomen immediately opened, a small piece of liver rapidly removed and dropped into 5 cubic centimeters of a 40 per cent solution of sodium hydroxide, which had previously been placed in a 50 cubic centimeter centrifuge tube and weighed. The tube with the sodium hydroxide and piece of liver was immediately reweighed to obtain the weight of the liver sample.

The time from stunning the pig until the liver sample was placed in the sodium hydroxide never exceeded one minute and as a rule was less than 30 seconds. Duplicate samples were run in each experiment.

The extraction of glycogen from the liver was carried out by Sahyun's modification of the Pflueger method. After extraction of the glycogen and its conversion into glucose, the latter was determined by the Somogyi modification of the Shaffer-Hartman method.

RESULTS

Control guinea pigs. The pigs used in this group were fed the standard diet for 6 to 19 days. They gained in weight and were in excellent condition at the time they were killed. The last feeding was given 24 hours before death although the animals ate food over a part of this period. The data from the animals in this group are given in Table I. Each pig gained in weight. The liver glycogen varied from 3.2 to 8.6 per cent.

Thyroid fed guinea pigs. The animals in this group received in addition to the standard diet 0.5 gram of desiccated thyroid extract[1] daily, after a trial period on the standard diet during which they gained in weight. The

[1] Parke Davis & Co.

TABLE I.—GLYCOGEN CONTENT OF THE LIVER OF CONTROL ANIMALS

No.	First weight gm.	Last weight gm.	Gain gm.	Liver glycogen gm. per cent
1	630	733	103	5.2
2	567	639	72	5.4
3	580	605	25	3.2
4	377	537	140	8.6
5	664	703	39	4.7

TABLE II.—THE EFFECT OF THYROID FEEDING ON THE GLYCOGEN CONTENT OF THE LIVER

No.	Weight before special feedings gm.	Days	Weight after thyroid gm.	Loss gm.	Liver glycogen gm. per cent
1	540	9	409	131	0.34
2	605	19	466	139	1.12
3	490	23	356	134	2.74
4	666	6	595	71	0.46
5	441	20	288	153	0.10
6	482	26	288	194	0.16

TABLE III.—THE EFFECT OF THYROID EXTRACT AND POTASSIUM IODIDE ON THE GLYCOGEN CONTENT OF THE LIVER

No.	Weight before special feedings gm.	Days	Weight after thyroid and iodine gm.	Loss gm.	Liver glycogen gm. per cent
1	493	16	298	195	0.05
2	402	16	283	119	0.12
3	455	11	289	166	0.10
4	459	9	325	134	0.11
5	577	6	391	186	0.23

TABLE IV.—THE EFFECT OF THYROID AND GLUCOSE FEEDING ON THE GLYCOGEN CONTENT OF THE LIVER

No.	Weight before special feedings gm.	Days	Weight after thyroid and glucose gm.	Loss gm.	Liver glycogen gm. per cent
1	389	5	322	67	0.12
2	543	7	441	102	0.25
3	435	6	346	89	0.15
4	560	6	462	98	0.18

data from this group are given in Table II. Every pig lost weight although the percentage loss in weight did not bear a constant relation to the degree of depletion of the liver glycogen. A striking feature in the thyroid fed pigs was the frequency with which exophthalmos developed.

Thyroid and potassium iodide fed animals. In addition to the standard diet on which the pigs were first fed, thyroid extract 0.5 gram and potassium iodide 10 minims of a saturated solution were added to each daily ration. While in every instance the pigs gained in weight on the standard diet they lost in weight when thyroid extract and potassium iodide were added to the diet (Table III). The loss of the liver glycogen was similar to that found when thyroid extract alone was added to the standard diet. There is no evidence that the iodide in any manner counteracted the effect of the circulating thyroid hormone.

Thyroid feeding plus glucose. We were especially interested in whether or not additional carbohydrate in the standard diet would, when thyroid extract was also fed, increase the liver glycogen. To each 16 grams of the standard diet, we added 4.8 grams of glucose (bactodextrose) and 0.5 gram of desiccated thyroid extract. The data in Table IV show that neither was the weight loss prevented nor was there a greater glycogen content in the liver under these conditions.

EVALUATION

The fact that thyroid hormone can effect a reduction or even what amounts to a depletion of the liver glycogen is now more or less generally accepted. It has been shown in our experiments that the rate and degree of the glycogen depletion bears no direct relation to the number of days over which thyroid feeding has been continued. If, in the human patient a similar course of events takes place, the importance of anæsthesia and other factors which still further deplete the liver glycogen and prepare a fertile soil for serious hepatic degeneration must be kept constantly in mind.

The ineffectiveness of iodine on the circulating thyroid hormone was pointed out by Kunde who did basal metabolic determinations on dogs fed thyroid extract and thyroid extract and iodine. The experiments which

we are reporting add additional evidence to Kunde's data and furthermore show that as long as the thyroid hormone gains access to the blood stream the liver stores of glycogen continue to be markedly reduced. The observations of Marine and of Frazier and Mosser that the beneficial effect of iodine in hyperthyroidism is the result of its effect on the thyroid gland itself would seem to be strengthened.

Of considerable importance are the data relating to the inability to increase the glycogen store of the liver during marked hyperthyroidism. It would seem that the effort to do this is wellnigh worthless unless the hyperthyroidism can be controlled either with iodine or operation or both.

Operation for hyperthyroidism without question throws an additional load on glycogen stores which are reduced in severely ill patients even under the best of conditions. Therefore, the value of attempting to restore the liver glycogen by the judicious use of carbohydrates immediately after operation should be emphasized. The intravenous method would at this time seem to offer the most rapid means of doing this in patients very ill after operation. In this regard the observations of Frazier and of North are extremely interesting.

CONCLUSIONS

1. The addition of thyroid extract to guinea pigs receiving a diet, which without the thyroid extract permits of a gain in weight, results in a depletion of the liver glycogen.

2. The addition of iodine to the diet of an animal receiving thyroid extract fails to prevent the depletion of the glycogen stores of the liver.

3. The addition of glucose to the standard diet of guinea pigs receiving thyroid extract fails to restore the liver glycogen.

4. The implications of these data with respect to the management of patients with hyperthyroidism have been pointed out.

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STUDIES IN BONE SARCOMA

III. An Experimental and Pathological Study of the Rôle of the Periosteum in the Formation of Bone in Various Primary Bone Tumors

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In the literature on primary tumors of bone, there is considerable discussion concerning histogenesis, especially in regard to new bone formation. As again pointed out in a previous article (2) the group of primary bone neoplasms characterized by extensive atypical new bone formation in the primary growth and similar new bone formation in the soft tissue metastases affords conclusive evidence for the existence of the osteoblast or bone forming cell, since these neoplasms represent a malignant degeneration of this cell. No other explanation can account for these tumors, much less the explanation offered by the humoral school of osteogenesis which maintains that new bone formation in osteosarcomata is the result of a reprecipitation in the tumor of calcium absorbed from the osseous site of the tumor growth (5). Brunschwig and Harmon (3) showed that injection of calcium in several forms into growing transplantable soft parts sarcoma did not induce new tumor bone formation. In addition to new bone of tumor cell origin, "reactive" bone, or bone not formed by the activity of tumor cells, is often described in various types of primary bone sarcoma. In the literature, there is little definite information concerning the source of this new non-tumor bone, its relationship to tumor bone and to the tumor cells. Many years ago Ribbert pointed out that at the margins of extracortical portions of tumors of central origin, there was an area of newly formed non-tumor bone. This, he stated, was due to elevation of the periosteum by the adjacent expanding tumor mass (*PL* in Fig. 12). These regions of newly formed non-tumor bone are always sought for in roentgenograms when the diagnosis of bone tumor is considered. These areas have been called "periosteal lipping" or "reactive triangles." Ribbert made no attempt to correlate the cell type of the primary tumor and the extent of periosteal lipping; nor did he attempt to determine a possible relationship between the elevated periosteum and new non-tumor bone formation *within* the tumor. The only additional observation made by this author was that tumor cells invading these "reactive triangles" destroy most of the newly formed non-tumor bone, leaving some fragments that are incorporated in the tumor mass as it expands in all directions.

The problem of the histogenesis of primary bone tumors would be greatly facilitated were it possible to cause malignant degeneration of a given type of cell in the bone of an experimental animal and compare the morphology of the resulting tumor with those observed in man. Such experiments not being technically possible at the present time, it was decided to mimic them by placing fragments of a transplantable mesoblastic tumor in various locations in bone, and observing the resulting neoplasm. These tumors correspond to the malignant degeneration in bone of mesoblastic cells which, themselves, do not form bone.

EXPERIMENTAL

The transplantable neoplasm employed which originated in the abdominal wall, is known as rat tumor 256, and was kindly furnished by Dr. Roscoe R. Hyde of the School of Hygiene of the Johns Hopkins University. Microscopically it is composed of round and spindle cells of various sizes, the latter producing collagen. Numerous mitotic figures are present. The tumor grows at first by expansion and later infiltrates the surrounding tissues. Regional lymphatic and pulmonary metastases are produced in the later stages of growth. Successful transplantation is pos-

sible to almost all species of rats in over 75 per cent of the inoculations. Tubes of Rosenow's beef broth and brain medium remained sterile for 3 weeks after inoculation with small fragments of the neoplasm. The tumor is not filterable, even through Berkefield-V candles. Young adult white rats were used in the experiments. All operations were performed under aseptic conditions and ether anæsthesia.

EXPERIMENT I

A. Small fragments of the sarcoma were placed beneath the periosteum of the shaft of the femur in three rats.

B. The knee joint was opened, a sharp probe forced upward into the medullary cavity of the femur through its distal articular surface, and an elongated fragment of tumor pushed into the central portion of the femoral shaft in five rats.

C. A minute opening was made in the anterior crest of the tibia about 1 centimeter from the knee joint and a small fragment of tumor inserted into the medullary cavity in ten rats.

Four weeks after implantation, the extremities operated upon exhibited large tumor masses arising from the bone that seriously interfered with the function of the member. The animals were sacrificed at this time and the tumor masses were found to surround the bone into which transplantations had been made. The tumor adjacent to the shafts contained newly formed bone but roentgenograms were unsatisfactory in demonstrating its pattern because of the fine structure. Blocks of tumor including the shaft of the bone were fixed in formalin, decalcified, embedded in celloidin, sectioned and stained by hæmatoxylin and eosin and by phosphotungstic-acid-hæmatoxylin (Mallory).

Microscopic examination (Figs. 1 and 2) reveals that the tumor has grown through the cortex producing areas of absorption. Beyond the cortex, the accumulation of neoplastic cells elevated the periosteum for some distance. Finally the tumor has grown through and beyond the periosteum. In that portion of the tumor between elevated periosteum and cortex there are fine trabeculæ of bone radiating at right angles to the surface of the shaft. Between the elevated periosteum and cortex there are numerous fine connective tissue strands. It is in these strands near the shaft that the new bone has been laid down, although on cursory examination it may seem that the bone was produced by metaplasia of the tumor cells (Fig. 4). Adjacent to the cortex these bony trabeculæ appear quite mature, but as they are followed peripherally they become less mature in appearance and finally become continuous with bands of osteoid tissue. The latter in turn are continuous with the fine fibrous strands that extend to the periosteum. These strands appear to be fibers of Sharpey that have become elongated as the periosteum was elevated and thus maintained their connections between this membrane and the cortex.

The newly formed bone differs considerably in appearance in different zones in the same section. In places there are well defined bony trabeculæ, similar to those of normal cancellous bone. Elsewhere, the bony trabeculæ are straight, long, and slender. There are also small areas in which recently precipitated calcareous granules are present about large rounded cells, forming a lace-like network in the intercellular spaces and presenting a picture not unlike the atypical tumor bone seen in malignant osteoblastomata in man (Fig. 4). Areas of cartilage are also present beneath the elevated periosteum in some of the sections (Fig. 5). Osteoid tissue, when present, is always between the most peripheral portion of the bony spicules and raised periosteum (Fig. 3).

In sections from some specimens, the periosteum is elevated over a considerable portion of the shaft, but there is not the extensive new bone formation throughout the subperiosteal zone as described above. Instead, there are scattered groups of radiating bony trabeculæ and irregular islands of bone and cartilage. There is no apparent explanation for the differences in quantity of new bone in the different specimens, although the extent of periosteal elevation was about the same in all cases.

It is stated above that the newly formed bone was of periosteal origin. This conclusion was based upon low power study of the

sections, in which all the bone was found to be present only in the subperiosteal portions of the tumor. However, from a microscopic study alone of the new bone under the higher powers, especially those areas of atypical bone, it is impossible to state definitely that the tumor cells do not become incorporated into the bone, since in many places they apparently can be seen in all stages of inclusion by bone as bone cells. Yet, if actual metaplasia of tumor cells into bone cells did occur a true osteoblastic osteogenic sarcoma would have been formed. This, however, was not the case (see Experiment 2).

In addition to elevation and stimulation of the periosteum to new bone formation, the tumor has also stimulated endosteal new bone formation. Short trabeculæ of new bone are present radiating into the marrow cavity from the inner surface of the cortex. The cortex itself, included within the tumor, shows scattered areas of absorption, a process likewise stimulated by growth of the neoplastic cells through it.

EXPERIMENT 2

Fragments of tumor including newly formed bone were obtained from the inoculated femur of some of the animals used in previous experiment and implanted beneath the skin, into the liver, the deep thigh muscles, and dropped into the peritoneal cavity of other rats.

Two weeks later the animals were sacrificed. Sections of the tumors revealed that the neoplasm had grown profusely, true to the original histological type. The fragments of bone were either completely absorbed or remained as small dead spicules in the centers of the tumor masses. Thus, this bone behaved as does an ordinary bone homotransplant to subcutaneous tissue. This is additional evidence that all the bone formed in Experiment 1 was periosteal in origin and that the bone cells were not tumor cells, although histological study might have warranted such conclusions. Had the tumor cells become bone forming cells, some of them would have continued growth as such in these transplants and have reproduced bone, just as it is produced in ossifying metastases from certain osteogenic sarcomata (malignant osteoblastomata).

EXPERIMENT 3

A segment of bone 3 millimeters long was removed from the midshaft of the femur in each of 10 young adult rats, the contents of the medullary cavity removed, and a small fragment of tumor pushed into the cavity. These segments were placed in the subcutaneous tissues of the flank in 10 other rats.

Three weeks later the tumors had become 2 to 4 centimeters in diameter. The rats were sacrificed and sections revealed that in 6 instances the segment of bone in the center of the tumor had died, the neoplasm growing about it as a soft tissue sarcoma. In 4 instances the bone transplant also died but there had developed spicules of bone radiating from the surface of the dead segment, similar to those seen in Experiment 1. The tumor had grown beyond and incorporated this new bone. Here, again, the new bone is formed from the periosteum which is elevated from the surface of the cortex by growing tumor. That in 6 instances no new bone formation is seen can probably be accounted for by the fact that revascularization of the osteoperiosteal transplant did not take place soon enough for survival of the periosteum.

EXPERIMENT 4

Periosteum was stripped from the femur from each of 5 young rats, wrapped about small fragments of tumor and placed in the subcutaneous tissues of other animals. Three weeks later, gross and histological examination of the resulting tumors revealed no evidence of new bone or osteoid tissue.

OBSERVATIONS ON PRIMARY BONE TUMORS IN MAN

In the experiments described it was demonstrated that malignant mesoblastic cells growing from bone and not possessing osteoblastic properties, may elevate the periosteum and cause it to form bone. This bone is present in the form of spicules radiating at right angles from the surface of the cortex and is laid down *in* the tumor within fine connective tissue strands that extend from elevated periosteum through the mass of neoplastic cells to the surface of the cortex. All stages of osteogenesis are present depending

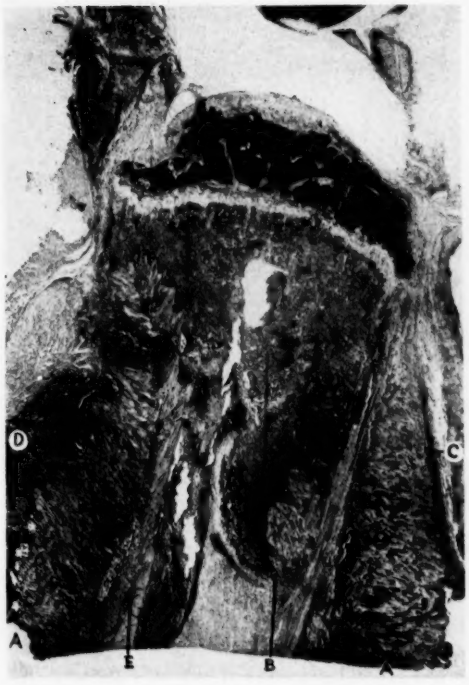

Fig. 1. Experiment 1. Photomicrograph of sagittal section through upper portion of rat tibia. A fragment of tumor had been implanted into the medullary cavity 4 weeks previously. The neoplasm has grown outward in all directions, through the cortex elevating the periosteum. *A*, Radiating trabeculæ of periosteal new bone within the extracortical portions of the tumor. *B*, Endosteal new bone formation. *C*, Elevated periosteum. *D*, Neoplasm that has extended beyond elevated periosteum and contains no new bone. *E*, Absorption of cortex by the neoplasm. ×12.

Fig. 2. Photomicrograph of cross section of rat tibia into the medullary cavity of which a fragment of transplantable sarcoma had been implanted 4 weeks previously. *A*, Elevated periosteum. *B*, New bone of periosteal origin in tumor. *C*, Tumor that has grown beyond elevated periosteum and contains no new bone. *D*, Cortex absorbed by growth of tumor through it. ×12.

upon the area inspected. A short distance beneath the periosteum osteoid tissue and islands of cartilage may be present. Nearer the cortex the bone is more mature. Adjacent to the cortex the bone resembles normal cancellous bone.

The pattern of new bone formation in these experimental neoplasms is quite similar to that seen in certain types of bone sarcoma in man, especially those forms of Ewing tumor in which there are fine strands radiating from the surface of the cortex. Soft tissue metastases from Ewing tumors do not produce bone, thus showing that all the bone in the primary neoplasm is of non-tumor origin.

Study of a large Ewing tumor of the upper half of the humerus removed from a 13 year old girl (Fig. 7), shows precisely the same general morphology presented by the tumors produced in Experiment 1. The neoplasm was apparently of central origin, grew outward through the cortex, elevated the periosteum for some distance from the shaft, stimulated osteogenesis, and finally grew through and beyond the periosteum. A study of the gross specimen (Fig. 7) shows the elevated periosteum with the new bone beneath it in the form of radiating trabeculæ. Roentgenograms (Fig. 8) show the uniform height of the trabeculæ, indicating also the limits of the elevated periosteum within the tumor.

Microscopic examination shows compact masses of round tumor cells situated between

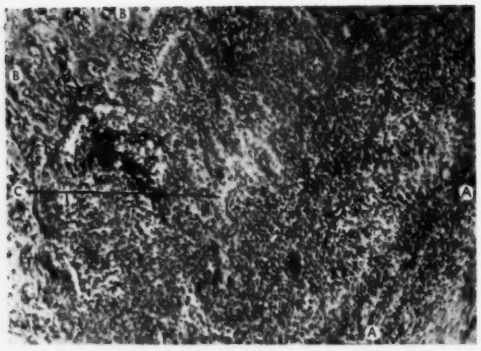

Fig. 3. Photomicrograph of a region in the extracortical portion of the neoplasm shown in Figure 2, showing *A*, elevated periosteum; *B*, new bone; *C*, osteoid tissue in region between elevated periosteum and new bone. ×75.

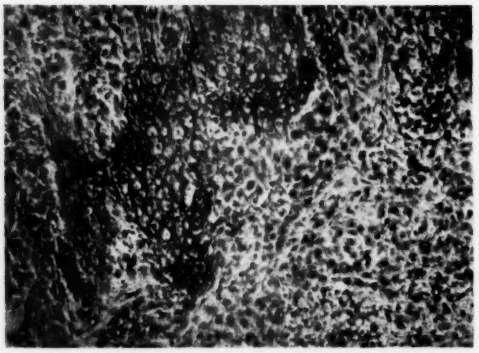

Fig. 4. Photomicrograph of another region of extracortical portion of tumor shown in Figure 2, showing calcareous deposits about cells. This is an early stage of new bone formation in the tumor, and from the histological examination alone it is not possible to state whether this is new bone of periosteal origin or whether it represents atypical bone of tumor cell origin. ×135.

the straight trabeculæ of non-tumor bone that extend to the elevated periosteum. There are no areas in which the tumor cells vary in type to become spindle shaped and to appear to undergo osseous metaplasia. Some authors (Kolodny), however, have incorrectly, we believe, stated that new bone in Ewing's tumors is both tumor bone and non-tumor bone. All Ewing tumors do not exhibit the radiating spicules of bone that give the so called "sun burst" effect in roentgenograms. Some of them, although of central origin, are predominatingly osteolytic and when the periosteum is elevated by them, they do not stimulate its osteogenic properties to any appreciable extent. Roentgenologically, such neoplasms are indistinguishable from fibrosarcomas of bone. The so called "onion" layers seen in roentgenograms of Ewing's and other neoplasms of bone is due, we believe, to alternating periods of rapid and slow growth. When the neoplasm grows rapidly, no new bone may result or there may be a few radiating strands. When there is a period of relatively slow growth, the periosteum has an opportunity to form a layer of

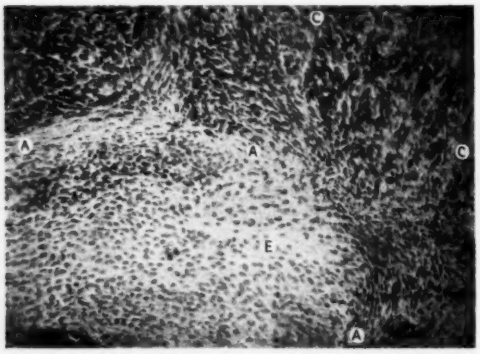

Fig. 5. Photomicrograph of extracortical portion of a bone sarcoma produced in experiment 1, showing *A*, elevated periosteum; *C*, tumor that has grown beyond the periosteum; *E*, an island of "tumor" cartilage. This cartilage is in reality of periosteal origin, formed by elevation of this membrane and quite analogous to the cartilage seen in the callus developing about a fracture. ×90.

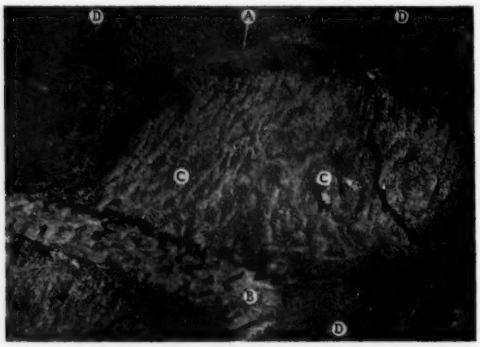

Fig. 6. Photomicrograph which illustrates experiment 3, a transplant consisting of bone and tumor, into soft parts. New bone *C* has been formed by elevation of *A*, periosteum from surface of *B*, a transplanted segment of femur. *D*, Neoplasm which is growing about transplanted segment of femur and which contains no new bone. ×25.

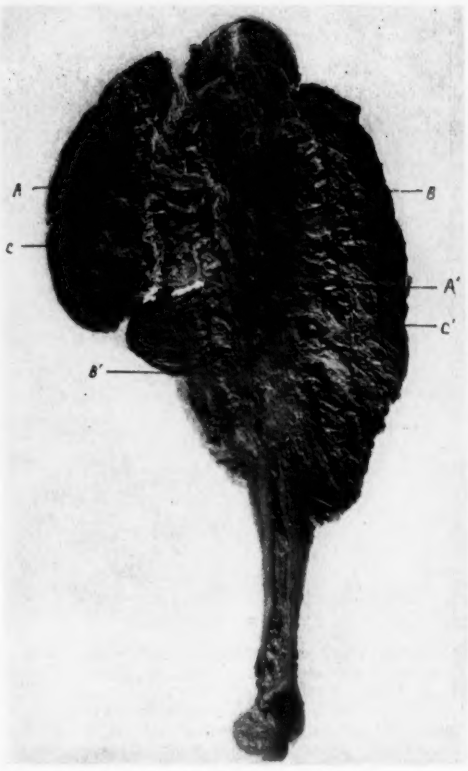

Fig. 7. Photograph of split humerus showing large Ewing tumor in upper portion. *A* and *A'*, periosteum elevated by expansile growth of tumor. *B* and *B'*, newly formed bone present as fine spicules radiating from the cortex of the shaft (Roentgenogram in the following illustration), and confined to the subperiosteal zone. *C* and *C'*, portions of the neoplasm that have grown through and beyond elevated periosteum and therefore contain no new bone.

Fig. 8. Roentgenogram of specimen of Ewing tumor primary in the humerus (specimen shown in Fig. 7), showing radiating trabeculæ of periosteal new bone. The rather uniform height of the radiating trabeculæ indicates the level of the elevated periosteum. The peripheral portion of the tumor does not contain new bone because it has grown through and beyond the periosteum. *PL*, Periosteal lipping, new bone formed by elevation and stimulation of periosteum by adjacent expanding tumor mass.

bone analogous to an involucrum in osteomyelitis.

In those osteogenic sarcomata in which the tumor cells themselves have osteoblastic properties as shown by their ossifying metastases to soft tissues, the greater part of the newly formed bone in the primary growth is of tumor cell origin. Yet, periosteal elevation may also be an important factor in new bone formation in the primary tumor as in the following case: A densely ossifying osteogenic sarcoma in the upper end of the tibia produced ossifying metastases in the inguinal lymph nodes and lungs. There is extensive new tumor bone formation throughout the intramedullary and extracortical portions of the tumor as shown in Figure 9 which is a roentgenogram of a sagittal slice of it. Figure 10 is a microscopic section of the slice. It shows the periosteum elevated posteriorly over the tumor by the expansile growth of the extracortical portion. Much new bone formation of periosteal origin is also present in the tumor. Study of the deepest regions of the extracortical portion of the neoplasm shows bony trabeculæ, extending from the cortical surface that are obviously of periosteal origin, having been laid down as this membrane was being elevated by the expansile growth of the tumor mass. In these deeper regions the periosteal bone is being absorbed by tumor in the same manner as is the normal bone of the shaft included within the tumor.

Fig. 9. Roentgenogram of slice of osteogenic sarcoma in upper end of tibia, a section of which is reproduced in following illustration. Note new bone formation in extracortical and intramedullary portions of tumor. The new bone in the extracortical portion is both of periosteal and tumor cell origin.

Fig. 10. Photograph of sagittal section 25 micra in thickness from osteogenic sarcoma in upper portion of tibia. There were also ossifying metastases in the inguinal lymph nodes and lungs. *P* and *P'*, Periosteum elevated posteriorly by expansile growth of tumor. *S*, Region from which higher power photomicrograph was made (see Fig. 11). *M* and *M'*, limits of intramedullary portion of tumor. ×1¼.

On microscopic examination of limited areas of neoplasms such as just described, mature bone of tumor cell origin may sometimes not be distinguished from non-tumorous mature bone (Phemister, 7). Conversely, as shown by the experimental tumors, there may be areas of new bone of periosteal origin that are very atypical (Fig. 4) and that resemble atypical bone of tumor cell origin. But where large sections are made through the entire neoplasm, the general topography of the newly formed bone in relation to periosteum and tumor cells is of considerable assistance in making a more accurate interpretation of the histogenesis of this bone.

Peripheral or periosteal osteogenic sarcomata arise from malignant degeneration of osteogenic cells (osteoblasts) in the periosteum or peripheral portion of the cortex. Figure 13 is a roentgenogram of a sagittal section through the lower third of a femur bearing such a tumor. The neoplasm, apparently arising in the posterior surface of the bone did not extend inwardly; the marrow cavity is free from tumor. Instead, it had literally wrapped itself *about* the lower portion of the shaft and infiltrated adjacent muscles and fascia. Microscopic examination shows it to be composed principally of mature bone and large islands of hyaline cartilage some of which are undergoing ossification. This specimen illustrates how a peripheral osteogenic sarcoma involving periosteum at its point of origin may grow about other portions of the shaft *on top of the periosteum*. Thus the new bone within it, although in this case of mature appearance, is entirely of tumor cell origin since the periosteum was not elevated. Figure 14 is a section from region *S* of Figure 13, showing the cortex with its periosteum

Fig. 11. Photomicrograph of peripheral area of extracortical portion of osteogenic sarcoma in upper end of tibia, taken in region indicated in Figure 10. *P*, Periosteum that has been elevated by expansile growth of tumor. *PB*, Periosteal new bone formation overlying peripheral margin of tumor. *TB*, Atypical bone of tumor cell origin situated within masses of neoplastic cells. *PB'*, Trabeculæ of periosteal bone that were formed as periosteum was being elevated by expansile growth of tumor. The spaces between these trabeculæ are now invaded by neoplastic cells and this bone of non-tumorous origin is thus situated within the neoplasm itself, and alternates with areas of atypical bone of tumor cell origin (*TB* and *TB'*). ×6.

Fig. 12. Photomicrograph of section through upper margin of a central osteogenic sarcoma in lower portion of femur. *PL* (Periosteal lipping), triangular area of new bone of periosteal origin due to elevation of *P*, periosteum by *S*, expanding extracortical portion of osteogenic sarcoma. *BD*, Zone of invasion of periosteal lipping by tumor cells, with destruction of the periosteal bone. *TB*, Bone in tumor. Some of this bone is of periosteal origin and some of it is true tumor bone formed by the osteogenic activity of the tumor cells themselves. *C*, Cortex of femur. *M*, Medullary cavity. *MT*, Intramedullary portion of tumor containing bone of tumor cell origin and endosteal origin. ×2⅛.

in place and ossified tumor *on top* of the periosteum.

Chondrosarcomata of bone are the result of malignant degeneration of chondroblasts. Areas of new bone of tumor cell origin and calcified tumor cartilage are irregularly distributed within them. These represent maturation of certain portions of the tumor (6). When arising centrally, these neoplasms may finally perforate the cortex and form large extracortical masses. Figure 15 is a roentgenogram of a slice of the upper portion of a tibia bearing a large chondrosarcoma. Irregular scattered masses of ossification and calcification are seen. In the inferior portion of the extracortical mass, fine strands of bone radiating from the cortex are present. Gross and microscopic study showed that the periosteum was reflected over the tumor mass, having been elevated from the surface of the cortex. These fine radiating strands are composed of nontumor bone, having been laid down within and about the tumor by the periosteum as it was elevated and stimulated by the expansile growth of the tumor.

Fibrosarcomata of bone are osteolytic. When arising centrally, they first destroy the cortex and then by expansile growth elevate and later disintegrate the periosteum. Over such tumors the undestroyed elevated periosteum exhibits little or no osteogenic activity. If a few new bony trabeculæ are laid down, they are immediately attacked by eroding tumor cells and osteoclasts and are destroyed. Figure 16 is a microscopic section from the periphery of a fibrosarcoma arising in the upper portion of the tibia showing the beginning destruction of small bony trabeculæ that were formed by the overlying elevated periosteum.

An interesting phase of the question is the factor or factors that govern the osteogenic activities of the periosteum when it is elevated by these neoplasms of various cell types. As was pointed out, some of the neoplasms composed of malignant osteoblasts and some Ewing's sarcomata stimulate a high degree of periosteal new bone formation *within* them. Chondrosarcomata cause only a very limited amount of such new bone formation. Fibrosarcomata, certain osteogenic sarcomata and some Ewing's sarcomata, although elevating the periosteum extensively, may stimulate very little or no new periosteal bone formation.

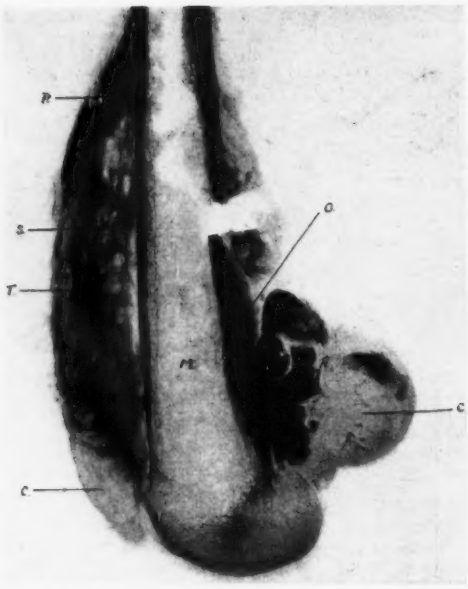

Fig. 13. Roentgenogram of slice of periosteal osteogenic sarcoma (malignant osteoblastoma) arising over lower portion of femur. *O*, area of periosteum or superficial region of cortex from which the neoplasm arose. *C*, Large mass of cartilage with areas undergoing ossification. *M*, Medullary cavity free from neoplasm. *T*, Portion of neoplasm that grew about shaft *on top* of periosteum and cortex. *P*, Narrow clear zone between tumor and surface of cortex denoting the presence of periosteum that has not been elevated from cortex. *S*, Area from which the microscopic section shown in Figure 14 was taken.

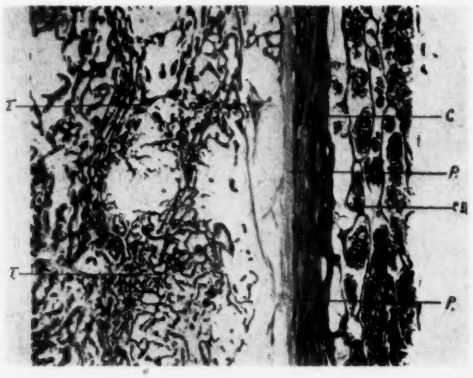

Fig. 14. Photomicrograph from area *S* in previous illustration. *T*, Bone forming sarcoma. The bone of tumor cell origin has a very mature appearance in this region. *P*, Periosteum lying on cortex in its natural position. *C*, Cortex. *CB*, Cancellous bone (bone sawdust is present in some of the marrow spaces). ×4½.

Not enough information is at hand to explain this relationship between these tumor cells and the osteoblastic activity of the periosteum and endosteum. Such new bone formation might be excited by mechanical disturbance, as from elevation and stretching of periosteum by the expanding tumor. It might also be excited biochemically by substances of tumor cell origin. That the periosteum tends naturally to form new bone when simply elevated is shown by the fact that at margins of the extracortical portion of these tumors periosteal lipping is always present to some extent.

In conclusion, mention may be made of the recent work of Berg in which a filterable tumor producing agent was injected into the medullary cavities of the tibiæ in chickens. In the resulting neoplasms there were fine, closely applied trabeculæ of bone radiating from the surface of the cortex. A study of the illustrations accompanying this report shows that the bone is entirely of periosteal origin, due to the elevation of this membrane by the expanding tumor, as in the experiments described above, and not due to osteoblastic properties of the tumor cells, as inferred by this author.

SUMMARY AND CONCLUSIONS

1. A transplantable rat sarcoma originating in the abdominal wall, the cells of which do not exhibit osteogenic properties, was inoculated into the medullary cavity (and beneath the periosteum) of long bones. The neoplasm grew through and considerably beyond the cortex, elevated the periosteum and caused it to lay down new bone in the form of radiating trabeculæ within the tumor.

2. Additional experimental evidence is also presented to show that all of the new bone in these tumors was periosteal in origin and not due to osteoblastic properties acquired by the tumor cells as a result of implantation within bone.

3. In osteogenic sarcomata (malignant osteoblastomata) in man elevation of the periosteum by the growing neoplasm may be an important contributing factor to new bone formation even though the tumor cells themselves also exhibit osteogenic properties.

Fig. 15. Roentgenogram of slice of chondrosarcoma arising in the upper portion of the tibia. *TB*, Scattered areas of tumor bone and calcification are present in the extracortical mass. *PB*, Fine radiating strands of periosteal bone.

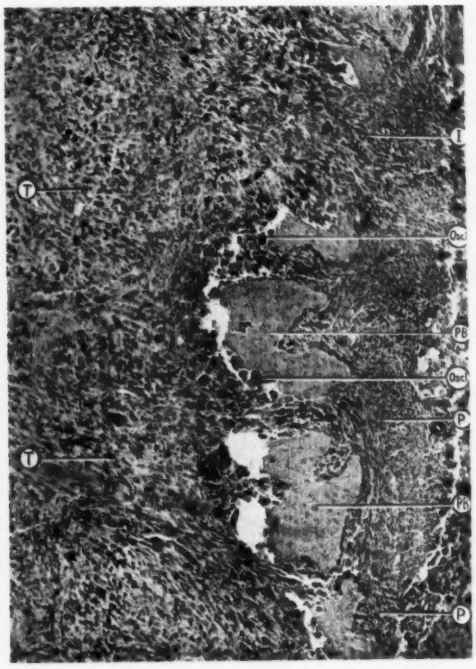

Fig. 16. Photomicrograph of peripheral margin of fibrosarcoma arising in upper portion of tibia. *T*, Tumor. *PB*, Trabeculæ of periosteal bone formed by elevated periosteum, *P*. These trabeculæ are being destroyed by erosive action of tumor cells and by osteoclasts (*Oscl.*). *I*, Invasion of tumor cells through the periosteum. ×70.

4. In Ewing's sarcomata, metastases to soft tissues do not ossify; yet within the primary growth there may be strands of bone, radiating from the cortex. All of this new bone is of periosteal origin, being laid down as the tumor elevates this membrane by expansile growth. The mode of new bone formation in this type of neoplasm is quite analogous to that in the experimental tumors described. The "onion" layers of new bone in Ewing tumors are also of periosteal origin.

5. In the extracortical portions of chondrosarcomata, fine spicules of bone radiating from the cortex may be present. These are of periosteal origin in contrast to the irregular areas of calcification and ossification that are scattered within the neoplasm and that are of tumor cell origin.

6. When periosteum is elevated over the osteolytic fibrosarcomata of bone, its osteogenic properties are little, if at all, stimulated.

7. There is no apparent explanation for the variation in osteogenic activity on the part of the elevated periosteum which is seen in the several types of primary bone tumors which have been described unless this activity rests in the biochemical properties of the tumor cell.

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LYCOPODIUM GRANULOMA[1]

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BY the term lycopodium granuloma is meant a granulomatous lesion developing in certain tissues after operation as the result of the introduction of lycopodium spores into the field of operation. Of recent years in many hospital operating rooms it has been the custom to use a dusting powder for gloves composed of a mixture of lycopodium spores and talcum powder: this is apparently an excellent preparation for the purpose. It is easily sterilized, keeps the gloves dry and serves as a lubricant so that they may easily be pulled over the hand.

Lycopodium powder consists merely of the spores of a species of club moss, Lycopodium clavatum which belongs to the fern family. While the plant is native to Europe, Asia, and America the spores for commercial purposes are collected chiefly in central Europe. The powder which has been called also vegetable sulphur, is pale yellow, smooth, fine, very mobile, floating on water and not wetted by it, and burning with a quick flash when thrown into a flame. Talc is magnesium silicate which is rather an inert material. In powder form this has rather a soapy feel and is an excellent dusting powder and lubricant. The ease with which lycopodium spores gain entrance to the tissues during the course of an operation requires no explanation. In the cases here reported granulomatous lesions were found around lycopodium spores, which had evidently been implanted in the tissues during previous surgical procedures.

The lesion is essentially a foreign body reaction to these spores, the spores themselves having been killed during the process of sterilization. It is composed of granulation tissue arranged in the form of nodules about the foreign body. The older nodules bear a striking resemblance to tuberculosis, showing endothelial cells, multinucleated giant cells, varying degrees of fibrosis and lymphocytic infiltration, with sometimes areas of necrosis or caseation. The spores may be found in the granulation tissue, the areas of necrosis, or in giant cells. They are hollow, spheroidal bodies measuring about 30 microns in diameter with scalloped or serrated margins and protruding from the surface are numerous spinous processes. When intact the outer surface presents a dimpled appearance not unlike that of a golf ball. On cross section they appear as a ring and contain a coarsely granular material. In hæmatoxylin and eosin sections they stain poorly; however, with the Ziehl-Neelsen preparation they stain a brilliant red.

REPORT OF CASES

CASE 1. A. R., male, aged 5 years, had suffered from chronic bronchitis and maxillary sinusitis for several years. He attended the out-patient department of the Hospital for Sick Children in 1932. In August of that year his antrum was irrigated repeatedly and on one occasion was injected with iodized poppy-seed oil. He returned about one year later with his symptoms persisting. In October, 1933, a radical antrum operation was performed and fragments of antral mucosa were sent to the laboratory for examination. The microscopic appearance of the lesion is shown in the accompanying photomicrographs. The general picture, as seen in Figure 1 is that of a conglomerate "tubercle" with fibrosis and peripheral lymphocytic infiltration. In the centers of the "tubercles" can be seen endothelial cells, multinucleated giant cells, and, in one instance, a small oval, pale staining granular spore. Figure 2 shows another "tubercle" with central caseation and one of the spores stained acid fast.

[1]Read in part before the Laboratory Section of the Canadian Public Health Association, Toronto, December 22, 1933, and before the American Association of Pathologists and Bacteriologists, Toronto, March 29, 1934.

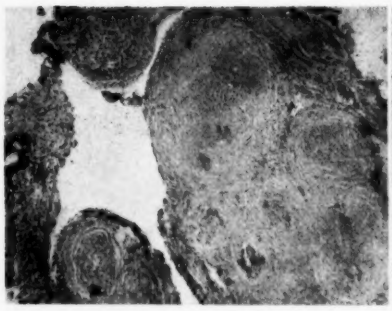

Fig. 1. Case 1. Maxillary antral mucosa, hæmatoxylin and eosin. ×35.

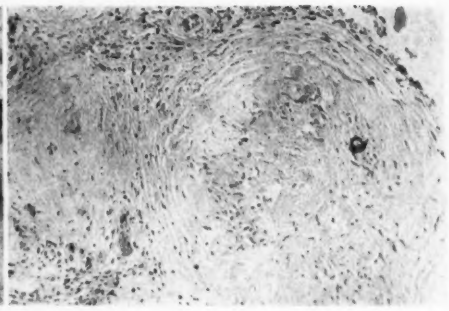

Fig. 2. Case 1. Ziehl-Neelsen followed by hæmatoxylin and eosin. ×105.

The tissue in this case was examined some 14 months following previous surgical treatment at which time it would appear that the spores were introduced.

Case 2. B. B., male, aged 9 years, was admitted to hospital December 8, 1931, and died April, 26, 1932, of cirrhosis of the liver of about 8 months' duration, 3 months following an exploratory laparotomy at which operation the liver was palpated. The lycopodium lesions, which were confined to the surface of the liver, were not noticed at the time the sections were first studied, and it was only during a review of our cases of cirrhosis of the liver, some months later that the true nature of these superficial lesions was recognized. The microscopic picture bears a striking resemblance to that seen in Case 1. (Figures 3, 4, 5.)

Case 3. This patient developed symptoms of intestinal obstruction 2½ years following appendectomy. A second laparotomy was performed by Dr. D. E. Robertson, to whom I am indebted for the clinical notes and the biopsy material, and with whose kind permission this case is being reported. Old adhesions were found at the site of the previous operation. These were severed and the symptoms relieved. During the operation several small, whitish nodules were seen studding the peritoneum in the ileocæcal region. One of these was removed for section. Its microscopic structure is shown in Figure 6. While the general appearance is similar to that in the 2 previous cases, the fibrous tissue is more dense, and caseation is more extensive. This may be accounted for by the longer interval of time (2½ years) which had elapsed between the two operations.

Case 4. W. K., male, was first admitted to hospital November 23, 1931, at the age of 10 years, for appendectomy. At that time the appendix which contained a number of pinworms, showed no evidence of acute or chronic inflammation and the boy made an uneventful recovery, his temperature falling to normal 48 hours after operation. He was readmitted February 21, 1934, with typical signs and symptoms of intestinal obstruction of about 24 hours' duration. The abdomen was opened and the obstruction was found to have occurred as the result of adhesions around the site of the previous operation. About 12 inches of small bowel was gangrenous. This was resected. Scattered over the peritoneum in the neighborhood of the adhesions were numerous small, whitish nodules. One of these was removed and its microscopic structure is shown in Figures 7 and 8. Following the second operation the patient made an uneventful recovery.

Case 5. A boy, D. L., aged 7 years, died of a malignant endothelioma of the pleura. Because of pressure on the spinal cord resulting from invasion of the spinal canal by the tumor, a laminectomy was performed. Five weeks later the boy died and examination of the tissues in the region of the operation revealed a granulomatous reaction with numerous foreign body giant cells, some "tubercle" formation and here and there the presence of lycopodium spores. In addition, however, to the spores there were also present small spicules of bone and what appeared to be the remains of suture material.

Case 6. A. S., male, aged 12 years, died in the Hospital for Sick Children August 15, 1933, of an abscess in the left frontal lobe. Two months before his death this abscess had been drained and a rubber drainage tube had been inserted. At autopsy the brain tissue immediately surrounding the tube bore little resemblance to cerebral cortex. There was proliferation of glia cells with some polymorphic infiltration. In addition there were quite numerous foreign body giant cells in which an occasional lycopodium spore could be found.

DIAGNOSIS

While, as stated above, these lesions bear a striking resemblance to tuberculosis, the essential feature in the diagnosis is the finding of the foreign body nucleus. To this end one must be familiar with the appearance of the spores. This, while quite characteristic as shown, may readily go unrecognized on superficial examination as the spores stain

Fig. 3. Case 2. Lesion on surface of liver, hæmatoxylin and eosin. ×120.

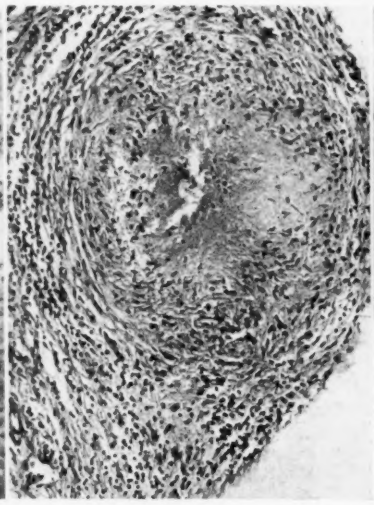

Fig. 4. Case 2. An unstained spore can be seen in the center of the area of caseation, hæmatoxylin and eosin. ×120.

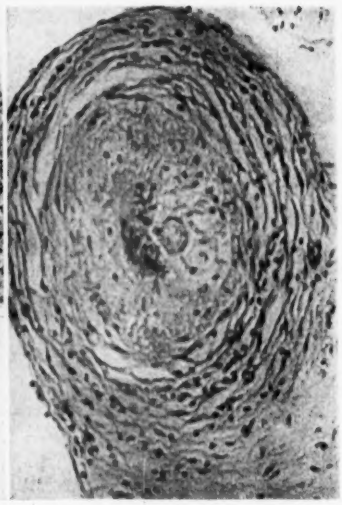

Fig. 5. Case 2. Ziehl-Neelsen, hæmatoxylin and eosin. ×200.

very poorly in routine hæmatoxylin and eosin sections. In doubtful cases the acid fast stain should establish the diagnosis. Because of the striking resemblance to tuberculosis, one must not be led astray by the presence of caseation, as this may be fairly extensive (Fig. 6). On the other hand it should be pointed out that the mere finding of a few lycopodium spores in a given section does not necessarily mean that they are the cause of the lesion. Because of their peculiar reticulated surface they readily adhere to any tissue, so it is quite conceivable that biopsy material might become contaminated by spores from the surgeon's gloves at the time of its removal. In this case they might be found around the periphery of the tissue. In order to incriminate the spores as the causative factor in a given lesion they must be found within the giant cells, or, at least, within the nodules of the lesion. The question as to whether or not the tissue under investigation has been the site of a previous operation should also be borne in mind. Another important factor is the locality of the lesion; for example, tuberculosis of the antrum would be extremely rare without evidence of clinical tuberculosis in other parts of the body.

LITERATURE

The literature on the subject of foreign bodies in general is rather extensive. The reaction in the surrounding tissues apparently varies with the nature of the tissue and with the size, shape, and chemical composition of the bodies themselves. Under the title of "Nodular Lesions of Peritoneum," Haythorn recently reported a series of nearly 30 cases, chiefly foreign body granulomata due to animal parasites, extravasated blood, gelatinous substances, oils and free fats, extruded stomach and intestinal contents and extraneous foreign bodies. Under the latter group he includes "sutures, threads, bits of sponge and so on," but while his article is very comprehensive, only four lines are devoted to this group in which no reference is made to lycopodium. The same appears to be true of all the other articles dealing with foreign body lesions, with the exception of a recent article by Antopol. He reports 6 cases and refers to 2 others; his photomicrographs show lesions almost identical with those reproduced here. He also mentions that similar lesions may be produced by talc crystals. Thus far we have not encountered any such in human material.

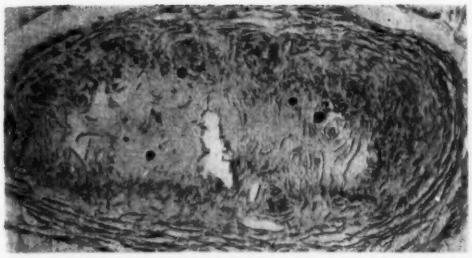

Fig. 6. Photomicrograph in Case 3. Ziehl-Neelsen, hæmatoxylin and eosin. ×50.

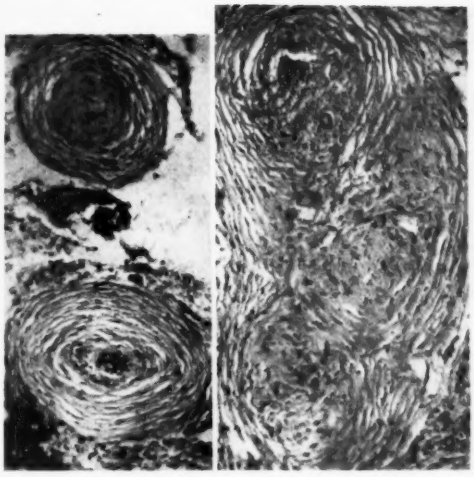

Fig. 7, left. Case 4. Hæmatoxylin and eosin. ×90.
Fig. 8. Case 4. Three spores can be seen in the upper half of the field. Ziehl-Neelsen, hæmatoxylin and eosin. ×90.

DIFFERENTIAL DIAGNOSIS

It is my purpose to draw attention to a type of lesion, the significance of which in the past has, no doubt, frequently been unrecognized.

Lycopodium powder has been used in the past to produce foreign body granulomata in experimental animals. This being the case, one need not be surprised, if such lesions develop in the human body after their accidental introduction into the field of operation.

As the title might suggest that one is dealing with some sort of fungus disease, it should probably be emphasized here that the reaction is essentially a foreign body one, the spores having been killed by sterilization previous to introduction into the tissues. That it is only a foreign body reaction, however, is another matter. The fact that the spores are acid fast, as are also tubercle bacilli, and that the lesions produced by the spores are almost identical with tubercles, even to the production of caseation, leads me to believe that the chemical composition of the spores may be an important factor in determining the type of reaction. According to the United States Dispensary, lycopodium spores contain "48.5 per cent of a neutral non-drying oil, very similar to almond oil. This oil contains 2 per cent of a fatty acid called lycopodic acid (C_{18} H_{36} O_4), 80 per cent of oleic acid, a minute quantity of a vegetable cholesterin similar to that obtained by Hesse from Calabar beans, 8.2 per cent of glycerin, and 3 per cent of arachidic, palmitic and stearic acids." It is no doubt this oily structure of the spores that causes them to burn with such a rapid and bright flash when thrown into a flame. That such a chemical composition should influence the type of reaction is more than probable. This view would seem to be supported by recent experimental work of Gardner and Cummings, working with silica and aluminum oxide. By intravenous injection into rabbits of fine particles of both these substances, these investigators were able to produce a "typical hyaline nodular silicotic fibrosis" of the liver by means of silica, while the same sized particles of aluminum oxide were merely phagocytosed and produced no fibrosis. They conclude their article in the following words: "These observations support the viewpoint that the injury produced by silica is specific and chemical rather than physical in character." The same, I believe, is true of lycopodium spores.

While lycopodium spores are obviously capable of producing lesions in the tissues, such lesions are not to be regarded as necessarily injurious to the patient. Of the 6 cases here reported, in 3 (i.e., Cases 2, 5, and 6) the course of the disease was probably in no way modified by the presence of lycopodium granulomata. The same, however, can hardly be said of the 3 other cases. In Case 1, it is quite possible that the presence of the spores in the antral mucosa may have produced an aggravation of symptoms. When one recalls that the an-

trum of a 5 year old child is, at best, quite small, anything that tends to produce a thickening of the mucosa might conceivably interfere with adequate drainage from the antrum. It is also conceivable that if spores were present in the wall of a discharging sinus, they might tend to cause persistence of symptoms. Cases 3 and 4 were similar in that both developed intestinal obstruction some 2 years after a previous appendectomy. That the adhesions which gave rise to the obstruction were caused in whole or in part by the lycopodium spores is difficult to determine. In Case 4 particularly, the gross and microscopic appearance of the appendix and the postoperative course on the first admission would lead one to believe that had no spores been introduced there would have been no cause for adhesions to develop. Following the discovery of this case, the use of lycopodium spores in dusting powder in this hospital was discontinued. In the last 2 cases reported, the lesions found cannot be considered as due solely to the lycopodium spores. In Case 5, while spores were found in the granuloma at the site of operation, other foreign bodies in the shape of chips of bone and suture material were also present. In Case 6 no spores could be seen in the field showing the greatest foreign body reaction; their presence, however, within the tissues served to illustrate the ease with which they may be introduced into the field of operation.

Thus, while the presence of the spores in some instances may give rise to little or no inconvenience to the patient, they may lead to serious errors in diagnosis which may result in radical or unnecessary surgery. Antopol reports the case of a man who was admitted to hospital because of a persistent sinus and mass in the epididymis. He gave a history of operation for traumatic hydrocele 2 months previously. A clinical diagnosis of tuberculous hydrocele was made and an orchidectomy was performed. Microscopic examination proved the lesion to be a lycopodium granuloma.

SUMMARY

Six cases of lycopodium granuloma are here reported, in which the spores were obviously introduced into the tissues during some previous operative procedures. In 4 of these cases the resulting lesions bore a striking resemblance to tuberculosis with which they might easily be confused.

Two of the patients developed intestinal obstruction from adhesions at the site of a previous operation, and there is reason to believe that these were caused by the lycopodium spores. In the opinion of the author the use of lycopodium spores as a dusting powder in operating rooms should be discontinued.

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FACTORS CAUSING DELAY IN OPERATIVE THERAPY OF CARCINOMA[1]

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THIS study was based upon interviews with 95 patients. This is, perhaps, a small number from which to draw conclusions, yet each case has been investigated personally by the author. All of the patients, with 3 exceptions, were admitted to the surgical wards of the Presbyterian Hospital in New York City. Of the 3 exceptions, 1 was a private patient and the 2 remaining were seen in the Out-Patient Department of the Vanderbilt Clinic. In all of the 95 cases a complete history and physical examination had been recorded upon the patient's chart. They were collected during a period of slightly more than 1½ years from October, 1929, to June, 1931.

Practically every group of cancer patients studied shows a marked period of delay between the onset of symptoms and the time that they obtain proper treatment. It is the purpose of this study to determine what are the chief factors causing this delay. It is generally considered that cancer in its beginnings is a localized growth. Whether this be absolutely true or not makes no great difference. It is true that in many and possibly even in the majority of cases the growth remains localized for a brief period of time. This is one of the peculiarities of cancerous tissue that gives us some ray of hope, namely, that we may possibly be able to eradicate the entire malignant tumor before any metastases have taken place. Without this hope, there would be very little to look forward to in the treatment of cancer except the use of surgery or radiotherapy solely for palliative measures.

Simmons and Daland in Boston analyzed the cases of malignancy of all kinds entering the Massachusetts General Hospital from 1917–1918 and 1921–1922 and found that there was an average of 12.5 months and 11.6 months, respectively, between the onset of symptoms and the appearance of the patient at the hospital. In the breast cases alone, there was an average delay of 11.4 months and 12.4 months, respectively, which is slightly greater than that found in the group of breast cases considered in this paper. J. M. Wainwright speaking on the reduction of cancer mortality states that the Pennsylvania Cancer Commission showed that "... in superficial cancers, while the patient himself was aware of his condition for 1 year and 2 months, the physician also had that knowledge for an average of 1 year. In deep-seated cancers the patient knew of the condition for 18 months and the physician knew of it for 13 months." Such delays are not limited to the State of Pennsylvania, but have been and still are prevalent in every state in the country.

To return to the causes of delay, we may ask, "What is to be considered as proper treatment?" The answer is that proper surgical treatment in cases of malignant disease where surgery is applicable is *radical treatment*. In other words, cancer is a deadly disease if untreated, if maltreated, or if given the correct type but inadequate amount of treatment. I mean by this that there are many patients that might have been saved had they been seen early and given radical treatment at the start.

The causes of delay in any group of cancer patients receiving what may be considered proper and adequate treatment are many, but these may be classed under four main headings: ignorance or carelessness, fear, expense, and lack of symptoms and disability. *Ignorance* may be blamed upon the patient himself, upon his family, relatives or friends, and upon his local physician or the physicians seen in hospitals or clinics. *Fear* may be that of the patient toward the disease or toward the possibility of an operation. Fear of a member of the patient's family for the patient may, in rare instances, cause considerable delay. The *expense* of examination or of treatment (including operation) may keep a patient from consulting a doctor or from entering a hospital. The *lack of symptoms and of disability* is seen in a great many cases as a cause for

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delay. Much of this delay is the result of lack of serious symptoms, or lack of pain. How many times have we heard a patient, when questioned concerning his duration of symptoms, remark, "It never bothered me, so I didn't think it serious and paid no attention to it."? More will be said about these causes of delay farther on.

The 95 cases were as follows: Carcinoma of the female breast, 41 cases; carcinoma of the rectum, 19 cases; carcinoma of the sigmoid colon or splenic flexure, 10 cases; carcinoma of the stomach, 8 cases; carcinoma of the cæcum, 6 cases; squamous cell epithelioma of the oral cavity, 5 cases; and a miscellaneous group of 6 cases. This miscellaneous group consisted of one squamous cell epithelioma of the lateral neck region, one squamous cell epithelioma of the auricle, one carcinoma of the œsophagus, one sarcoma of the gastrocnemius muscle, one melanoma of the eye, and one angio-endothelioma of the thigh. Each one of these cases was considered malignant upon pathological examination except the first case, which was obviously clinically a far advanced carcinoma of the breast.

The time lost since the onset of symptoms varied from 4 days in 1 case to 7 years in another. Where the time between the onset of symptoms and admission to this hospital was 2 weeks or less, it is fair to assume that such a short time cannot be considered as any real delay. There were only 4 such cases in this group. There were 2 other cases with a duration of symptoms of only 3 weeks, and 2 more with a duration of only 4 weeks. The average duration of symptoms for the whole group was 11.6 months. This latter figure is identical with that found by Simmons and Daland for the year 1921–1922. If our figures are at all comparable, it shows that there has been no appreciable improvement in lessening the pre-operative duration of symptoms in cancer patients.

ANALYSIS OF GROUPS

A. *Breast carcinoma.* Of the 41 cases of carcinoma of the breast (all females), 25 had previously consulted physicians before coming to this clinic. Fourteen cases had consulted but one physician; 6 had consulted two physicians; 2 had consulted three physicians; and 1 had consulted twelve physicians. Twenty-three of this group of 25 patients had a definite palpable mass that had been noticed subjectively; 12 had some pain; 2 had consulted nurses in respect to the lump; and 2 had sought treatment from a druggist without relief. Six had received definite bad advice or only local treatment from physicians outside. Eight patients were definitely delayed by carelessness or ignorance of the physicians examining them before they came here. There were 3 such cases in our own hospital. One was a patient examined and treated in the out-patient clinic for dyspnœa and in whom the lump was noted in the breast on physical examination. No diagnosis was recorded in the chart and the patient was never referred to the surgical department. She then disappeared for 15 months to return with a hopelessly inoperable carcinoma with local and distant metastases.

The second case was examined in the out-patient clinic, and the lump in her breast was considered benign. She was not seen by an attending surgeon on the day of her examination, due to some error, and there resulted an extra delay of 4½ months before she was finally admitted for operation. The third case may or may not have been treated earlier, as she had noted a lump in her breast for only 5 months. It is interesting to note that 9 months previously she had had her heart and lungs examined in the emergency ward prior to taking a general anæsthetic for treatment of an injury. One month later she was admitted to the hospital for an operation on her eye. On neither of these occasions was any note made by the examining physician in respect to her breasts.

Nineteen of the 41 patients may be partially or wholly to blame for their own delay either from ignorance or procrastination. There were 16 patients with breast cancer who had not consulted a physician before coming here. Each of these had a mass that she had noted herself. Twelve had had some pain referable to the breast or arm. In 15 the patient's own ignorance was largely the cause for her delaying consultation and treatment.

Nine patients of the entire 41 gave fear of the expense as a reason for their delays; 5 of

them gave this as their chief reason. Fifteen stated that fear of an operation was one of their reasons for delaying; 6 gave this as their chief reason. One patient, who had had a local removal elsewhere, gave the fear of a second operation as her chief reason for delaying further treatment after she had had a local recurrence of the tumor. None of these breast cases had any real disability attributable to the breast condition. In all but 2 the symptoms noted by the patients were considered mild, and hence they put off seeking medical advice for many months. Only 2 patients stayed away for fear that they might have a cancer.

In these cases of breast cancer there was an average delay of 10 months between the onset of symptoms and the time the patient was admitted for operation (see Table I). There was an average delay of 3.2 months between the onset of symptoms and the time the patient first consulted her own doctor. The time lost between the first consultation with her doctor and the time she was admitted to this hospital for operation was 8.6 months on the average. The average delay from onset of symptoms when no outside doctor was consulted was somewhat less, namely, 7.3 months. This average delay is altogether too long if we hope to do any real good for the patients afflicted with breast carcinoma. It may be argued that some patients who consult a surgeon regarding a breast lump and have a radical operation for the same done within 1 or 2 weeks do not necessarily turn out to live the longest in the end. Some of these, no doubt, have extensive metastases in their axillary lymph glands or elsewhere at the time the lump is first noted in the breast. Of course, if such be the case, the chances for a long "cure" following operation are small. However, many of these patients do not have early metastases; and, again, some patients who have had a known lump in the breast for a considerable period of time, varying from many months to sometimes a year or longer, still do not have axillary metastases at the time of operation. If this average delay could be cut down, let us say, 30 to 50 per cent, there would unquestionably be a much larger number of 5 and 10 year arrests as a result.

TABLE I

Site	Number of cases	Average delay when no outside physician was consulted	Average delay between onset of symptoms and first consultation with a physician	Average delay between first consultation with a physician and operation	Average delay between first cancer symptom and operation
Breast	41	7.3 mos.	3.2 mos.	8.7 mos.	10.0 mos.
Rectum	19	7.0 mos.	4.8 mos.	4.7 mos.	9.1 mos.
Sigmoid	10	7 days (1 case)	3.4 mos.	3.2 mos.	6.5 mos.
Stomach	8	12.0 mos. (1 case)	2.9 mos.	6.6 mos.	8.1 mos.
Cæcum	6	12.0 mos.	5.3 mos.	8.6 mos.	13.3 mos.
Oral cavity	5	12.0 mos. (1 case)	0.8 mos.	9.0 mos.	10.2 mos.
Miscellaneous	6	(Not inclu	ded here as	a group)	

This does not, of course, apply solely to breast cancers, but is applicable to other types as well.

B. *Rectal carcinoma.* Of the 19 cases of carcinoma of the rectum, 17 had consulted one or more outside doctors or clinics; more than half of them had consulted two or more physicians. The patient's own ignorance in 15 cases was definitely responsible in part for the delay in obtaining proper operative therapy. Two gave fear of an operation as the chief reason for delaying and 2 more gave this as a contributing factor. Two likewise stated that fear of the expense was their chief reason for delay and 2 more gave this as a contributing factor. Nine patients (or more than half of the total number of the 17 who had consulted physicians) were treated symptomatically without having had a rectal (digital) examination made upon them. This is a deplorable state when such patients are complaining of symptoms referable, in the greater majority of instances, to the lower bowel. One such case occurred in our own out-patient clinic. She had been examined and had been followed there for 10 months with increasing constipation as one of her complaints. The tumor in her rectum was only discovered at the end of this time when she was finally referred for surgical consultation, and the first rectal examination was made, and the tumor easily palpated. Another case in the hospital had

been proctoscoped and the mass in his rectum biopsied. Clinically at proctoscopic examination "the mass had the typical picture of a carcinoma." The biopsy specimen was sent to the laboratory where it was diagnosed incorrectly as a "benign polyp." The patient was allowed to go home, but his symptoms became more severe. He was finally readmitted 3 months later with a mass in his rectum that had increased to about three times its original size. Another biopsy specimen examined in the same laboratory was again diagnosed as "benign polyp." A similar piece examined by another laboratory was diagnosed carcinoma. The patient was operated upon, and an infiltrating carcinoma was found which had involved the adjacent lymph glands.

One patient was seen by three outside physicians none of whom had performed a rectal examination. The first of these was an insurance company physician who, when asked by the patient what to do for his increasing constipation, advised him to take mineral oil. He did no rectal examination although he was examining a patient who was taking out a life insurance policy. Another patient had been seen by five outside physicians, all of whom she stated were "specialists." One of these advised and performed a hæmorrhoidectomy upon her without having done a proctoscopic examination. She was naturally not relieved of her condition, but was caused an unnecessary delay of 8 months.

Space does not permit going into each case individually, but these just cited may help to show what is happening in a relatively large percentage. Six of the 9 cases which had received no rectal digital examination had easily palpable tumors. The 3 others had tumors that were discovered without difficulty when proctoscoped in this hospital. Of the nine, 8 had symptoms that called for a rectal (digital) examination, and the ninth had suggestive symptoms.

Lack of symptoms and lack of disability were of considerable importance in the delay of these rectal cases. In spite of this fact, many of these patients had a number of symptoms such as pain, constipation or diarrhœa, bleeding per rectum, etc., they also had had a definite change in their bowel habits which might have made them suspect something more than hæmorrhoids or colitis. There was only one patient of the 19 who really had severe symptoms and was actually disabled by her condition. One other patient was prevented from having an operation by his private physician and his wife, even after carcinoma of the rectum had been confirmed both by proctoscopic examination and biopsy in our clinic.

In these rectal cases there was an average delay of 9.1 months between the onset of the patient's symptoms and his admission to the hospital for operation. The time lost between the onset of symptoms and the first physician consulted averaged 4.8 months. That between his first consultation and his admission here for operation averaged 4.7 months. Only 2 patients came to the hospital who had seen no outside physicians. The duration of their symptoms was 2 months and 12 months, respectively.

C. *Carcinoma of the sigmoid colon.* Ten patients were studied with carcinoma of the sigmoid colon (in which is included 1 case of carcinoma of the splenic flexure). Nine of these consulted one or more outside physicians. Five had definitely received bad advice or treatment by these local physicians. In 8 of these cases the delay may be attributed in part to the patient's own ignorance either in not consulting a physician sooner or in not asking for a more complete examination with the assistance of X-rays. One patient stated that fear of an operation was his chief reason for delay. Two others attributed the fear of an operation as one of their reasons for delay. In only one of this group was fear of the cost of treatment responsible for the patient's delay. More than half of all these patients had symptoms of constipation, diarrhœa, or bleeding per rectum which really called for X-ray diagnosis by the adjunct of the barium enema. The X-ray is not always conclusive, as proved to be the case with one patient followed in our own hospital and clinic for 8 months before repeated X-ray examinations finally showed an obstruction in the sigmoid colon. The one case not seen by any outside doctors came to the hospital with symptoms

of complete obstruction for 7 days. On repeated questioning he stated that he had never had any symptoms prior to this attack of pain and obstipation. Two patients had been observed at other hospitals in New York City, but when advised to have exploratory operations they refused because the diagnosis was not considered certain. It is only natural not to accept an exploratory operation on an uncertain diagnosis, but had the necessity for exploration been impressed more firmly on the patient, he might have accepted it sooner.

One case in this group with symptoms of 7 years' duration had multiple polyposis of the colon and rectum and carcinoma of the sigmoid colon. It is hardly conceivable that operation for the polyposis at the onset would have cured him or prevented him from getting more polyps which might develop into carcinoma at a later date. For this reason this one case is omitted in calculating the statistics on delay in this group. The average duration of symptoms was 6.5 months. The average delay between onset and the first consultation with a physician was 3.4 months. The average delay between the first consultation and admission for operation at this hospital was 3.2 months. Early obstructive symptoms in these cases seem to account for the shorter delay as compared to the cases of rectal carcinoma. Lack of symptoms as well as only partial disability played a greater part in these delays than they did in either the breast or rectal cancers.

D. *Carcinoma of the stomach.* Although a small group, this collection of 8 cases shows many pathetic instances in which early diagnosis and operation might have prolonged the patient's life very considerably and most of all would have relieved his symptoms for many months. There were 6 of these who put off seeing physicians early or who kept putting off an exploratory operation until very late. Only one patient attributed his delay in part to the fear of expense. None actually stated that the fear of the operation itself made him delay in seeking and obtaining adequate treatment.

Only one patient had not consulted an outside physician. His own family physician had died, and he stated that he had no faith in any other. Consequently, he undertook to treat his increasing indigestion himself, as he did not think his condition at all serious. Of the 7 remaining, 5 were definitely given bad advice and treatment by outside physicians. Of the 2 others, both had been followed and treated in our own clinic or hospital. The first, a 60 year old woman, with digestive disturbances, had been followed for 3½ years in the out-patient clinic. Her symptoms and signs were indefinite, the X-ray findings negative, and it was deemed inadvisable to operate with so little evidence pointing to a definite lesion. At the end of this time, a final X-ray showed "two ulcers of the stomach" and the patient was finally admitted for operation. Such a delay cannot be attributable to lack of keenness on the part of the physicians, for she was seen frequently during this period and nothing positive could be found until very late. It is also unlikely that this patient's symptoms were due to a carcinoma for 3½ years. An ulcer was most probably the original lesion, but unfortunately this could not be demonstrated at a time when operative therapy had much to offer.

The second patient, a 56 year old man, came to the hospital complaining of an inguinal hernia. At the time of his admission he had some vague gastric symptoms for which a gastro-intestinal X-ray examination was done which showed an "ulcer." He was then explored. A mass was felt in the pyloric end of his stomach which was thought by the operator to be "carcinoma or ulcer induration." One firm lymph gland was also felt near the pylorus. No biopsy was taken. A gastro-enterostomy, entero-enterostomy, and appendectomy were then done. The patient finally returned 5 months later with symptoms of obstruction. At this time a second exploratory operation revealed metastatic nodules of tumor tissue scattered all over the peritoneum and a large mass in the stomach. No one can be dogmatic about the prognosis in individual cases, but it seems highly probable that this patient might have been greatly benefited by resection of the pyloric portion of the stomach at first operation had the operator not taken the chance of its being "ulcer induration."

Disregarding the one case of 3½ years' duration, the average delay in these gastric cases was 8.1 months from onset of the symptoms to admission to the hospital. The average delay between onset of symptoms and the first consultation with a physician was 2.9 months. The delay between the first consultation and admission here for operation averaged 6.6 months. With very few exceptions, all these patients showed symptoms that were moderate or mild and none showed any real disability. Cancers of the stomach like cancers elsewhere show an insidious onset which explains the great delay in these patients seeking early treatment. Being so called internal cancer, it is not easy to see how much improvement will take place in hastening these cases to get early diagnosis and adequate operative treatment.

E. *Carcinoma of the cæcum.* Again this is a small group of cases (six), but each one delayed seeing a physician or refused what was considered adequate treatment when prescribed by a physician. Two had seen no physicians outside of this institution. Three were given definite bad advice or treatment by the physicians consulted. One was treated by her physician for pernicious anæmia for 2 years. When she did not improve he advised having intestinal X-ray pictures taken on several occasions, but his hands were tied by the patient who refused these on account of the expense. The fault in this case was not entirely his, as he presumably was considering the patient's finances. On the other hand, it unquestionably cost the patient more in the end, and had he insisted on the X-rays, he not only would have saved her money, but would have been able to establish the diagnosis much earlier. One other patient in this group gave the fear of cost of treatment as her chief reason for delay. Another attributed the fear of an operation as a contributing reason for her delay.

The total average delay from onset of symptoms to admission to the hospital in these cases of carcinoma of the cæcum was 13.3 months. The average delay from onset of symptoms to the first consultation with a private physician was 5.3 months. From this first consultation to admission for operation in this hospital the average delay was 8.6 months. The 2 patients seeing no physicians prior to coming to the hospital, each showed a duration of symptoms of 12 months. The delay in these cases is naturally longer than in those having carcinoma of the sigmoid. This is due largely to the different physiology of this portion of the bowel where fluid fæces easily pass until the obstructing lesion becomes very marked. Other clinics have noted similar findings.

In only 3 of the 6 cases were symptoms shown that might be considered mild and their mildness acted as a contributing factor in their delay. None of the 6 showed any real disability.

F. *Squamous-cell epithelioma of the oral cavity.* There were 5 patients in this group. One had been in this hospital a year previously but her tongue at that time was giving her no trouble. She noticed nothing until after she had left the hospital, and then did not consult a private physician or come back to have her tongue examined in the hospital until after nearly 1 year, when she then had a definite epithelioma. This patient gives her sole reason for delay as being due to fear of the expense. Of the 4 remaining patients, 2 had seen at least 2 physicians and dentists and 2 had seen at least 3. Two may blame their delay to a considerable extent to their own ignorance. One of these consulted a druggist and received treatment from him for several months before seeing a physician. All 4 were definitely given bad advice and treatment by the dentists and physicians they consulted. Of these, 1 was treated with local applications for 7 or 8 months on a diagnosis of Vincent's angina, while the lesion which had first healed reappeared and became progressively worse under treatment. No biopsy had been taken. The second was treated with a small dose of radium in another hospital without a biopsy having been taken. He then went to a second hospital where a biopsy was taken and the patient referred to this institution. It might be argued that X-ray or radium was the proper treatment in this case. Even if this be conceded, the dosage was most likely inadequate and in addition was not based on microscopic examination of a biopsy specimen. The

third case was seen by several dentists. He had three biopsies taken, the first two of which showed "benign papilloma," the third was lost. Finally, after 10 months when an X-ray picture showed an "infectious process in the mandible," the patient was referred to this hospital. The fourth case had a local removal 1 year previously by an oral surgeon, following which he was given either X-ray or ultra-violet light treatment. The lesion finally recurred 4 months later, but the patient put off going to see his dentist again for 3 more months. The latter then sent him to this hospital.

The average time lost in these cases between the onset of symptoms and admission to this hospital for operation was 10.2 months. All of the patients, with one exception, consulted a dentist or a physician within 2 months or less after the onset of the first symptom. The average delay between the first consultation with a dentist or a physician and admission to this institution for operation was exactly 9 months in the 4 cases that had sought any medical advice outside. Four of the 5 patients had little or no symptoms and no disability. This may account for some, but not all of their delay. The fifth patient had much pain and also disability. He sought treatment early and persistently. He, however, was the one who had had two "negative" biopsies and a third one that was lost and was only referred to us after 10 months of local treatment.

G. *Miscellaneous cases.* Since each case in this group is of a different type, it is felt that a brief summary of the individual case would be better than trying to sum them up as a whole. It will thus be seen more clearly where the delay took place and to whom it may be attributed. The first case, a 33 year old woman, had a tumor in her neck for 2 years. She went for 18 months without consulting a physician. A friend had told her it was an "enlarged gland" and was of no significance. Finally, when she consulted a physician he gave her "injections" for 3 months without relief. The tumor turned out to be a squamous cell epithelioma of the lateral neck region (the growth probably arising from a branchiogenic rest).

The second case was that of a 37 year old woman with a tumor of her lower thigh of 3 years' duration. She had been treated by four private physicians without a diagnosis having been made, and without relief. She was afraid an operation might be necessary and for this reason stayed away from hospitals and clinics. At last a friend told her she might have a tumor and advised her to see another physician. This she did (at the end of 3 years) and was referred to this hospital. Her tumor turned out to be an angioendothelioma.

The third case, a 55 year old man, who had suffered for 7 months with difficulty in swallowing and a loss of over 60 pounds in weight, consulted no physicians outside of this hospital because he "did not think his condition amounted to anything," and because he was afraid of the expense. He turned out to have a carcinoma of the œsophagus. There may be some doubt about early treatment being of benefit in this case, but it shows how a patient can neglect himself in spite of marked symptoms.

The fourth case, a 71 year old man, came to the hospital complaining of double vision, occasional pain, and bulging of his right eyeball. The double vision had been present for 3 years. He saw a physician shortly after the onset who treated the condition with eye-drops without relief. Later he consulted an eye clinic where he was likewise treated with eye-drops. One physician at this clinic had suggested an operation, but the patient states that "this never came to a final decision." He later saw three other physicians in turn, and each of these treated his eye with drops. Following this he went to another hospital where a small dose of radium was given without relief. Finally, at the end of 3 years, when his eye began to bulge, his daughter insisted on his coming to this hospital. His condition was due to a malignant melanoma that had broken through the sclera and had invaded the posterior part of the orbit, thus forcing the globe forward. Although the patient had paid little attention to his condition, even though it did not improve, a careful ophthalmoscopic examination early would probably have clinched the diagnosis and led to early adequate treat-

TABLE II.—PERCENTAGE SURVIVAL RATE OF CANCERS WITH AND WITHOUT AXILLARY METASTASES AT OPERATION (AFTER STOUT)

	Three years postoperative		Five years postoperative	
	Alive	Apparently cancer-free	Alive	Apparently cancer-free
No metastases	63.0	47.5	54.0	46.0
All cases	46.9	25.0	32.5	23.3
Metastases	38.9	14.5	22.3	12.3

ment. The majority of the physicians seen by the patient were general practitioners who had merely made very superficial examinations of the eye and then proceeded to treat it symptomatically.

The fifth case, a 33 year old woman, consulted a physician 14 months previously for pain and cramps in the calf of her leg. He treated her for "fallen arches," but the pain persisted, though not severe. One year later she consulted another physician because the calf of the leg had become swollen. This physician incised the swelling in the belief that she had an abscess, but found no pus. He took no biopsy and told the patient that he had found "nothing suspicious." When she came to us, a microscopic section showed a reticulum-cell sarcoma of the gastrocnemius muscle for which amputation was done.

The last case was that of a 56 year old man with a squamous cell epithelioma of the auricle, which he had had for 2 years. He treated it himself for 6 months without success. He then consulted a physician who spent 12 months more treating it with salves and lotions, but without success. At last the physician took the patient to a specialist who immediately referred him to this hospital.

SUMMARY

The lack of symptoms and the lack of disability play by far the greatest rôle in delaying cancer patients in seeking and obtaining what is considered proper and adequate treatment. Many of these patients have perfectly definite symptoms of their disease, but it is a lack of severe symptoms or a lack of real disability that makes them not complain. This is the one characteristic of cancer, particularly in its early stages, that seems to be the "bugbear" of the medical profession in shortening the delay in these patients getting early treatment. As long as cancer rarely gives marked pain or other pronounced symptoms in an early stage, it will remain particularly difficult to get patients to seek earlier consultation unless more impressive propaganda is distributed to the lay public. Two patients only in this group came to the hospital because of hearing or reading about cancer symptoms. Both were breast cases. One, after attending a lecture on cancer, came to the clinic for advice concerning a lump she had had in her breast for 30 months. The second with a lump in her breast of 3 years' duration had consulted twelve physicians, but had been reassured by each in turn that the lump was of no importance. She finally read several articles in the newspaper and then came to the clinic.

The more specific causes for the delay in these 95 cases may be attributed to the patient's own ignorance of such conditions in 33 instances. In 19 cases it may be attributed to the patient and the physician combined. In 18 cases it may be attributed to the physician alone, and 5 of these were the fault of carelessness or ignorance of the physicians in this institution. This is but a small portion of the total, yet these mistakes might easily have been averted had a little more care been taken. It is easy enough to blame outside physicians for failure to recognize or treat a cancer properly when the case finally comes to a large hospital with all its personnel and diagnostic facilities, but it is regrettable when a similar inability to make a correct diagnosis (and especially in some fairly obvious cases) is due not so much to ignorance or stupidity of the physicians in a large hospital or medical center, but to carelessness on the part of these physicians in failing to do a rectal examination in a case of rectal carcinoma or when the volume of clinic routine and "red tape" cloud or delay the issue with resultant delay in the patient receiving a thorough and careful examination and early operation.

There were only 11 patients in the total number who gave the fear of cost of treatment as their chief reason for delay. Another group of 10 patients stated that the fear of an opera-

tion was their chief reason for not seeking relief at an earlier date. Only 2 patients in the whole group stated that they delayed because of the fear they might have a cancer.

The average lost time for all these patients studied was exactly 11.6 months. The author has attempted to estimate roughly the amount of delay that might have been avoided in each case. This estimated *avoidable* delay was approximately 7.6 months on the average. If it were only possible to eliminate this *avoidable* delay, it would mean that these patients would come to the hospital with an average *unavoidable* delay of only 4 months. It is interesting to speculate on the increased number of operable cases could they be obtained with such a short duration of symptoms.

There is a very striking difference in the results of various cancers treated before and after lymph node involvement has taken place. To mention the group of breast cancers alone, I could do no better than to quote Stout and reproduce the table in his book on *Human Cancer*. In a detailed analysis of all types of cancer operated upon at the Presbyterian Hospital for the ten year period of 1916–1925, inclusive, he states that "... there were metastases in 53 per cent of those cancers radically removed 1 month or less after discovery, and if one year or more had elapsed between discovery and operation we found that 73 per cent showed axillary metastases and 85 per cent later died of generalization."

Stout also states that "... if axillary nodes are involved at the time of operation it is an indication that the woman has less than one chance in eight of having had all the cancer removed by the operation, for only 12.3 per cent were cancer-free after 5 years. Conversely, if there are no axillary metastases found at the time of operation more than one-half the cases will survive more than 5 years and nearly one-half the cases will be cancer-free at that time."

CONCLUSIONS

In conclusion it might be well to repeat that the average total duration of symptoms in this series was 11.6 months, a figure identical with that found by Simmons and Daland, and nearly the same as that found in a study by Farr, namely, 11.9 months. Although it was the purpose of this study to determine the factors causing this delay, these factors in themselves would suggest a partial solution for shortening this delay. The fault was found to belong to the patient, the physician, or a combination of both in 70 cases in this series, or approximately 74 per cent of the whole group. It would seem, therefore, that anti-cancer propaganda for the lay public must be made much more effective if we are to expect patients to seek medical advice at an early date. On the other hand, this will be of no avail, unless even more strenuous propaganda be carried out within the medical profession in order to get the general practitioner to suspect cancer more frequently and to refer the suspected case to a surgeon or hospital well qualified to diagnose and treat cancer. When the *avoidable* delay can be cut down from one-half to two-thirds of its present length, then only shall we be able to expect a real improvement in the treatment of patients afflicted with cancer.

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CLINICAL SURGERY

FROM THE ST. HILDEGARD HOSPITAL

NEW METHODS IN GALL-STONE SURGERY

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THE general rules for operating upon an obstructed papilla do not differ very much in the different clinics of the world. If it is impossible to remove stones through a supraduodenal incision in the common duct, we usually try to extract them through a second incision in the retroduodenal part of the common duct, after extensive mobilization of the duodenum. We do not always succeed with this method either, in which case we resort to the radical method of laying bare the papilla across the duodenum.

Of course, we realize that by the two just mentioned methods, the retroduodenal and the transduodenal, the operative risk increases. The danger in the retroduodenal method lies in the fact that the tissue behind the duodenum has very little resistance to infections of any type. We note very often at postmortem examination a steady increase in infection in the retroduodenal region, in spite of the fact that it may have completely ceased in the intraperitoneal area. The retroduodenal region is also a favorable site for postoperative bleeding in the presence of cholæmia.

For all these reasons many surgeons have abandoned the retroduodenal operation completely in favor of the transduodenal route. The transduodenal route also has its drawbacks as we very well know, for it carries a high mortality rate, even if done by an able surgeon of long experience.

The operative risk increases as the infection and cholæmia progress. To judge from all large series of cases we are faced with untoward results in 50 per cent of the cases, and the risk is even greater in patients of advanced age. The surgeon is confronted with the knowledge that in spite of a perfectly executed operation he can do little to avoid many imminent complications.

In the following case I tried a new method which proved to be extremely successful, especially in view of the desperate condition of the patient who was in a state of cholæmia, and infection was far advanced.

A man, of 68 years, had suffered for years with gall stones. He recently had an attack of colic followed by jaundice which lasted for several weeks, and lately he has been having chills. He was brought to the clinic and we found the patient in a very bad general state. Besides sepsis and cholæmia he showed signs of an acute peritoneal irritation in the upper abdomen. Our suspicion that this was due to an acute pancreatitis was confirmed by the finding of large quantities of diastase in the blood. To have operated immediately would have given but little chance of success. Ice compresses were applied in the hope of localizing and diminishing the symptoms of general peritonitis. Fortunately, the symptoms did decrease during the following days, but a sudden flare up of all symptoms forced us to operate immediately.

I opened the abdomen through a costal incision (Figs. 1, 2, 3). A few words about this incision: It lies a little over the costal arch so that the base is formed by the costal bones. We can thus avoid all postoperative hernias with certainty, even in the presence of extensive suppuration. This could be proved during the 10 years this incision has been practiced in my clinic.[1]

After the peritoneum was opened numerous necroses in the fatty tissue were visible. The gall bladder was opened and numerous stones were removed. The badly inflamed mucous membrane of the bladder was quickly electrocoagulated (mucoclasis), the common duct was opened in the supraduodenal area, and many stones were extracted, but it was impossible to empty the papilla completely of stones through this incision. To carry on further manipulation by the retroduodenal or transduodenal routes would be taking too great a risk because of the general state of the patient, especially in the presence of acute pancreatitis.

I decided not to operate further at this time so simply introduced a small drain into the common duct, the drain reaching the stones. The common duct was then tightly sewed around the drain. Our idea was that should the patient survive we would try to dissolve the stones by the injection of suitable dissolving liquids by way of the drain. The operation was thus performed very quickly and the recovery of the patient was so satisfactory that, on the fifth day, we could begin with our experiment.

Daily injections of several cubic centimeters of ether were made upon the stones. Ether is one of the best soluble liquids for cholesterin. Our intention was to destroy the compact consistency of the stones by dissolving the cholesterin nucleus, thus reducing the stones to a soft pulp which would easily pass the papilla. That this can be done can be proved very easily by mixing the most ordinary bilirubin calcium stones with ether. The stones crumble

[1]Pribram. Der Costalschnitt. Deutsche Ztschr. f. Chir., 1930, 225. Zur Technik d. Costalschnittes bei Gallenoperationen. Zentralbl. f. Chir., 1934 No. 27.

into a sediment of brown, soft pulp, as can be seen in Figure 4. The cholesterin, after having been dissolved in ether crystallizes into white needles after evaporation (Fig. 5). It still remained to be seen whether or not this experiment could be practiced on a patient with the same success.

On the fifteenth day of the treatment it seemed for the first time that not all of the sodium chlorate solution injected returned but that some of it flowed through the papilla into the duodenum. An immediate X-ray examination after the injection of an opaque liquid confirmed my observation.

In Figures 6 and 7, the biliary ducts are seen filled with the opaque liquid, and over the papilla are two distinct spots showing the position of the remaining stones. It will also be noted that some of the opaque liquid has already passed into the duodenum. Another X-ray picture, taken several days later, during treatment with ether, shows that the papilla has been completely freed and nearly all the injected opaque liquid has passed into the duodenum.

It was now very easy to manipulate the drain through the free papilla into the duodenum (see Fig. 8). We extracted the drain and 3 days later the fistula on the abdominal wall had completely closed.

I have used the ether method in the 4 other patients who were sent to my clinic to be operated upon for papillary obstruction. All these patients were in very poor general condition with advanced cholæmia and sepsis and had been having frequent chills daily. In all of these patients the operation was completely successful. By means of the X-ray I was able to watch the progress of the freeing of the papilla as shown in Figures 9, 10, 11, 12, 13.

The injection of ether is borne by the patient generally without complaint. It is important, however, that not more than 2 or 3 cubic centimeters be injected at a time and that the tube should be left open after the injection has been completed or else undue pressure would be produced in the epigastrium, as a result of the evaporation of the ether which takes place at body temperature.

The value of this method seems to be twofold. The operation is very simple and can be done quickly; the operative risk, therefore, is greatly lessened as compared with the risk connected with other operative methods formerly in use. This technique seems to be especially indicated in patients suffering with cholæmia and sepsis, when the most simple operation is also the best one.

We use this method in place of the retroduodenal or the transduodenal method, not only in cases in which we are unable to free the papilla by simple incision of the common duct, but also in cases in which there is the least suspicion that all the concrements have not been removed. The ether dissolves stones even when they are embedded in the wall of the common duct, a position difficult to reach by mechanical means. This method has proved of value too in the treatment of biliary fistula caused by stones which were overlooked in the common duct when operation was first carried out.

The introduction of a drain through the fistula down to the stones and the application of ether, cause in a short time the softening and partial dissolution of the stones and their passage through the papilla. Thus a second complicated operation is avoided.

Other surgeons have also reported good results following treatment of biliary fistulas with this method. By means of the X-ray and the injection of iodized oil through the drain we are able to determine with certainty whether the papilla and the common duct are absolutely freed of stones before we remove the drain. The small remaining fistula will then close in about 24 hours.

This procedure will diminish the number of the so called pseudo recurrences.

A prolonged study of the causes of so called recurrences after gall-stone operations has convinced us that a considerable number of these complications are directly or indirectly due to loss of function of the resected gall bladder. Before explaining the new method of procedure, I would therefore like to summarize our findings concerning the function of the gall bladder as well as regarding the pathological and clinical manifestations following the loss of function.

One of the main functions of the gall bladder is to serve as an overflow reservoir, equalizing the oscillating pressure in the common duct and regulating this pressure. The liver does not produce bile continually, but in certain rhythmical stages bile is poured forth, the quantity produced being influenced by nutrition and other external causes. This interrupted secretion of the liver causes changes of pressure in the common duct but within certain limited bounds; much greater are the changes of pressure in the common duct produced by the rhythmical contraction of the papillary muscle, the sphincter of Oddi.

These changes of pressure can be studied very easily in a patient with a drain in the common duct. For this purpose the drain must be placed in such a position that its end will lie above the papilla but far enough from it so as not to interfere with the rhythmical play of the sphincter muscle. The wall of the common duct must be sewed tightly around the drain. The quantity of bile flowing out through the drain must be measured every hour.

We very often notice variations in the outflow of bile, the quantity varying from 0–20 cubic centimeters and even more. A large quantity indicates a closed papilla; while if the papilla is open all of the bile flows into the duodenum so

that the outflow of bile stops almost completely. Figure 14 is a curve showing the amounts of bile collected hourly and illustrates well the papillary function. The rise in the curve corresponds to the time when the sphincter was closed, the descent of the curve while the sphincter was open.

These oscillations in pressure are regulated perfectly through the natural function of the gall bladder which fills during the time the sphincter is closed. A constant pressure in the common duct is thus secured. When the gall bladder is destroyed by inflammatory processes, when the cystic duct is closed on account of the presence of stones, or when the bladder has been removed by operation, all the unregulated changes of pressure are then transferred to the liver.

Patients usually do not feel the changes in pressure except when the spasm of the papilla lasts a longer time than usual, when prolonged spasms of the spincter of Oddi are apt to occur. This has been observed in many patients.

That such prolonged spasms really occur I was able to determine clearly by means of the X-ray in the case of a woman whose papilla had been absolutely freed. The X-ray picture showed all biliary ducts filled with iodized oil with not a single drop passing through the contracted papilla. The spastic contraction of the papilla was maintained during the whole time of the observation, i.e., nearly an hour. After this I made an intravenous injection of 1 milligram of atropine sulphate. When it first became evident that the atropine had taken effect (dryness in the mouth and mydriasis) I made a new X-ray picture. The papilla was then wide open and the iodized oil was flowing in a wide stream into the duodenum. (Figs. 15, 16, 17.)

The patient whose gall bladder does not function properly feels the spasms as very unpleasant sensations in the region of the liver. His complaints are characteristic: a feeling of oppression in the upper abdomen, belching, nausea; also a temporary enlargement of the liver is noted. Many patients are constitutionally inclined to spasms of all kinds, but in addition we know that some external factors may act as irritants and cause spasms of longer duration: cold drinks, gastric and enteritic processes with or without ulcerations, constipation, and intoxication of alimentary origin.

An unregulated increase of the biliary pressure has a much graver effect in the presence of latent hepatitis; here reactivation of the hepatitis manifests itself in enlargement of liver due to œdema, increase of temperature, and even jaundice.

We find such attacks of hepatitis fairly often in the recurrent case. Critical observation of these cases shows that the flare up of such types of hepatitis has become more frequent after operation.

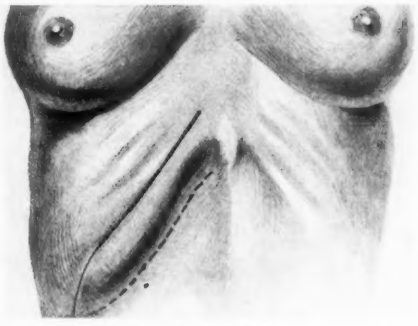

Fig. 1. Costal incision.

We must, therefore, conclude that in these cases the hepatitis has been aggravated by the cholecystectomy. The explanation of this fact is easily found if our previous statement is recalled: the gall bladder, the function of which is to regulate the bile pressure and to prevent stasis, is missing. In a certain sense the gall bladder acts as an organ to protect the liver. In addition, another fact should be mentioned; after the gall bladder is resected we find that the inclination of the sphincter of Oddi to spasms has in many cases increased and especially if the patient is constitutionally inclined to spasms generally.

The nervous regulation of the gall bladder and of the sphincter of Oddi are so connected that tonic contraction of the bladder is associated with the opening of the sphincter, whereas a contraction of the sphincter is co-ordinated with distention of the bladder. Such nervous connections are found in most organs limited by a sphincter, for instance the œsophagus, the urinary bladder, etc. I wish especially to emphasize the relation between the pathological narrowing of the cardia and the dilatation of the œsophagus. That relation is not simply the result of cause and effect but is based on common nervous disturbances. Removal of the gall bladder destroys the complicated nervous mechanism which regulates the bile ducts, and thus is produced a disturbance which in many patients is manifested by an increased inclination to spasm. The increase of pressure as a result of the absence of regulation and the stasis in the bile ducts has a noxious effect upon the latent infection of the liver.

These disturbances of nervous regulation after cholecystectomy are not manifested in all patients

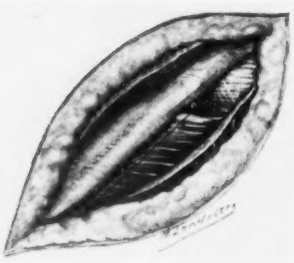

Fig. 2.

Fig. 3.

by a cramp of the sphincter; sometimes—and this is the second form of disturbance after loss of function of the gall bladder I wish to mention—a pronounced insufficiency of the sphincter is noted which causes a permanent flow of bile into the bowel.

These atomic forms of disturbances, as we shall call them, have their own clinical symptomatology: intestinal disturbances, ranking foremost; inclination to enteritis and diarrhœa; a diminished stomach secretion up to the point of complete achylia, etc. I have not the space here to enter into a discussion of all of these interesting problems, but I would like to mention the fact that we found that the use of pepsin and chloric acid was a means through which the intestinal disturbances which follow cholecystectomy may be overcome.

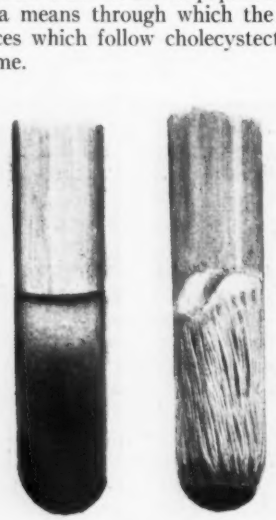

Fig. 4, left. Dissolutions of gall stones in ether.
Fig. 5. Dissolved cholesterine crystallizing, the ether having evaporated.

The gall bladder has still other functions of which I should like briefly to mention only a few. The concentrated bile of the gall bladder contains in large quantities activators for the digestion of fat. These activators are of the greatest importance; therefore the patient who has had his gall bladder removed is handicapped in the digestion of his food, especially of fat.

In addition, the gall bladder is an organ which probably produces in its mucous glands substances of hormonal character, which have a great influence upon appetite and palate, enabling one to discern and appreciate the different food-stuffs. I will later return to this subject.

Our experiences have therefore led us to be more conservative than formerly in resecting the gall bladder. We now resort to cholecystectomy only in those cases in which the gall bladder has been completely destroyed and its function therefore completely lost. Moreover, we are confronted with a new problem: not only to conserve the bladder but to restore its lost function if possible.

This problem led us to search for an operative method which would fulfill all the conditions which have been mentioned: the conservation of the gall bladder and at the same time the complete removal of gall stones, the avoidance of all recurrent troubles, the result of the loss of gall-bladder function, which function should be restored by operation. The operative methods designed to conserve the gall bladder which have been in use until now—cholecystotomy and cholecystostomy—do not by any means attain this end.

The follow up of patients who have been treated by cholecystostomy—an operation used rarely and only in special cases—has shown extremely bad results. We are not alone in the observations of these facts. I here mention particularly the

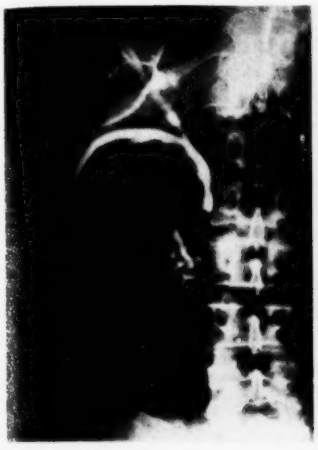

Fig. 6.

Fig. 7.

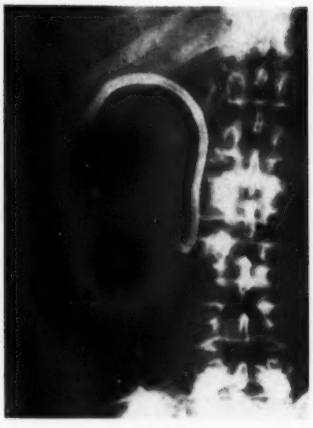

Fig. 8.

statistics of Whittaker and Spurling of Boston. Of the 12 cases observed, 5 patients had grave recurrent colics, 4 minor disturbances of different kinds, 1 had no liver symptoms but had a postoperative hernia, 2 patients only were without complaints. It should be mentioned, however, that these 2 cases had been followed for a period of only 25 days after operation. Six patients, that is half of all the cases, had to have a second operation. Four of these showed the formation of new stones, 1 had an acute necrosis of the pancreas, and all of them showed signs of cholecystitis.

Therefore, not only the danger of real recurrence, i.e., the formation of new stones in the gall bladder after cholecystostomy, is a big one but there are still other complaints. All facts led us to believe that cholecystostomy does not secure the result hoped for and therefore should be avoided.

The conditions which must be fulfilled in any operation to conserve the gall bladder are the following: In the first place, one must be sure to avoid every possibility of stasis in the gall bladder —the free outflow of bile from the bladder must be guaranteed. Stasis in the presence of infection is the main factor in the formation of new stones. Cholecystoduodenostomy and cholecystogastrostomy are also designed to avoid stasis in the gall bladder in that they include permanent drainage. Statistics showing the experiences of the later

Fig. 9.

Fig. 10.

Fig. 11.

Fig. 12.

Fig. 13.

results of this operation as published recently by many surgeons are not encouraging, however.

After a certain time it is found that nearly always a grave infection of the gall bladder follows the anastomosis with the bowel, an infection which not only revives the former symptoms of cholecystitis but also gives rise to an ascending cholangitis.

Cases have been observed in which, for instance after the gall bladder has been anastomosed with the stomach, the gall bladder had become a reservoir for remnants of food, thus causing very grave disturbances necessitating radical secondary operation. Such a case has recently been described by Enderlen. For all the reasons given we cannot use this operation in the presence of gall-stone diseases with the purpose of conserving the bladder.

I shall now discuss an operation which seemed to me to be worthy of trial. It insures the free drainage of the gall bladder, not by anastomosing it with the bowel or the stomach, but by effecting a wide anastomosis between the gall bladder and the common duct (Fig. 18). In this way the sterility of the bladder is preserved in spite of the very free outflow of bile; at least the bacteriological medium is not changed for the worse. At the same time the conditions for the healing of the inflammatory processes in the bladder are improved as the possibility of stasis is avoided.

Experiments have shown that the tendency of the gall bladder to heal after inflammation is not so small as we had thought. The gall bladder, moreover, is conserved with all its functions to regulate pressure and with all its normal secretion. It is really astonishing that, in spite of the clear logic of this operation, it has not previously been done.

It has always seemed to be the method of choice to operate upon a gall bladder with stasis (*Stauungsgallenblase*). The first case in which I attempted this new technique, cholecystocholedochostomy is an illustration. The history is interesting enough to be given in full.

A woman, aged 34 years, had suffered for years with pain under the right costal arch, nausea, and vomiting. She had been operated upon by another surgeon 2 years previously, on the suspicion of gall stone disease. There had been no pathological findings except a spastic contraction of the pylorus. For this reason a pyloromyotomy, i.e., a cut through the muscle of the pylorus, had been performed.

After the operation not only no improvement but a turn for the worse could be observed, manifested by a feeling of oppression, vomiting, and decrease of weight. The patient was rendered incapable of carrying on her professional duties and was sent to my clinic. The patient, very much reduced in weight, told us that for nearly a year she had not been able to eat anything without a feeling of fullness shortly afterward. She showed an intolerance of all food, not only of fat but also of meat and carbohydrates of all kinds. She could take only small quantities of food and remained in bed nearly all day. We found a distinct tenderness under the right costal arch. The suspicion that the complaints were due to ptosis of the stomach was not confirmed by the X-ray examination. Cholecystography revealed a badly filled bladder but of clear outline, emptying slowly.

Operation was done under spinal anæsthesia. The gall bladder was enlarged, was under much tension, and could not be emptied by pressure. The wall was thin and showed no signs of any grave inflammation. Adhesions between the neck of the bladder and the hepatoduodenal ligament caused a kink in the extremely long cystic duct. The bile secured by puncture showed the typical dark green color characteristic of that when stasis is present. I now effected in the manner mentioned, a wide anastomosis between the neck of the bladder and the common duct.

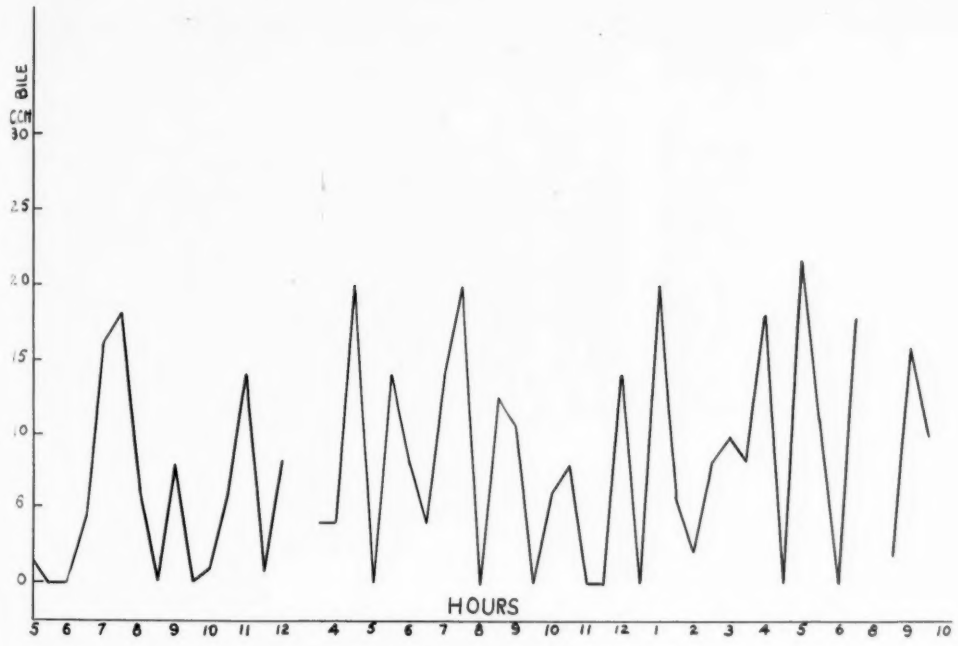

Fig. 14. Curve showing contraction of the papilla.

The effect of the operation was remarkable. The symptoms vanished almost immediately and the patient became astonishingly hungry within a few days after the operation—a surprising contrast to the constant lack of appetite before the operation. The further recovery of the patient was very rapid and she was able to eat any kind of food. Increase of weight was 15 pounds within a short time. During the whole time of further observation she never had any complaints.

To illustrate the improvement of the reabsorption of food further I should like to describe some experiments I made with this patient. It is known that for the digestion and the best reabsorption of fat not only the lipase of the bowel is needed but also the bile which increases the work done by the lipase in the sense of an activator.

According to our study the bile of the liver does not act nearly as effectively as does the bile of the bladder. The activating effect of the bladder bile sometimes surpasses the measure which could be expected from a more highly concentrated bile. From this fact it must be logically concluded that the bladder produces still other activating substances which perhaps are secreted by the glands of the gall bladder wall. And now to return to the experiments which were made in the case referred to:

Findings before the operation. In the duodenal juice large quantities of lipase were noted, but the activating effect of the duodenal bile was only slight. Digestion of fat was very poor. This was proved by the lack of a normal increase in the curve showing the bloodfat in the culminating point of digestion. Figure 19 shows a normal curve for blood fat during digestion with an increase in the culminating point nearly in the sixth hour after a meal. For comparison Figure 20 shows a flat curve which indicates poor reabsorption of fat. The activating value of the bile of the bladder secured by puncture during operation was extremely high.

To sum up: in spite of the fact that the duodenal juice contained a normal quantity of lipase and in spite of the fact that the activating value of the bile of the bladder was high, the activating value in the duodenal juice was very low. The digestion of fat was very poor as could only be expected when we realize that the bile of the bladder could not flow freely into the duodenum and thus its activating effect was lost.

After operation, i.e., after relief of stasis in the bladder and after the establishment of free drainage of the bile of the bladder into the duodenum, the duodenal juice obtained through a duodenal tube showed in contrast to our former finding a high activating value. Tolerance and digestion of fat became quite normal. This could be demonstrated by the presence of a normal curve as to blood fat. The favorable effect of all this on the patient has already been mentioned: an increase in appetite and a gain in weight within a short time.

Encouraged by the excellent result in this first trial I used the operation in several other cases with the following modifications in technique.

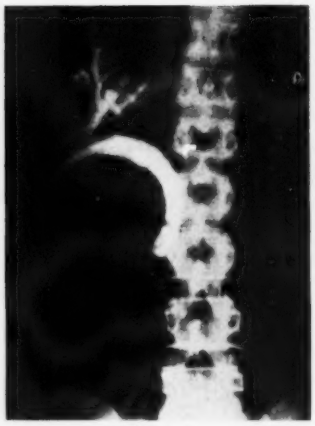

Fig. 15.

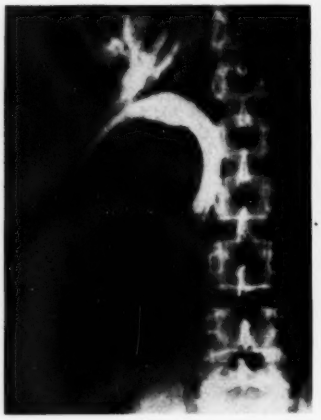

Fig. 16.

Fig. 17.

Fig. 15. Sphincter-muscle in contraction.
Fig. 16. Ten minutes later after having injected 1 cubic centimeter atropine. Sphincter begins to open itself.
Fig. 17. Few minutes later. The sphincter is now widely opened. There is present a free outflow into the duodenum.

The region is laid bare through the costal incision described. The gall bladder is punctured and its liquid contents are removed, and the bladder washed out with a solution of sodium chlorate. After the anterior wall of the common duct is prepared and after the small blood vessels which are nearly always found in this part are ligated, the common duct is opened through an incision 2 to 3 centimeters long. Calculi if found are removed and it should be determined definitely that the papilla is perfectly free. Then the bladder is opened in the upper interior wall by an incision just wide enough to remove all stones present. A new incision is then made in the neck of the bladder, the incision being made the same length as that in the common duct. Two catgut sutures fix the ends of both incisions and draw together the walls of the common duct and the bladder. While the assistant distracts the two holding sutures, suture of the posterior part of the anastomosis can be done very easily. In the same way suture of the anterior part of the anastomosis is perfected. The suture line is protected by serous tissue from the neighborhood, especially from the hepatoduodenal ligaments.

When signs of more grave inflammation in the bladder are noted or when many small stones are found, it is advisable, before the anterior suture is completed, to introduce through the bladder and the anastomosis into the common duct, a small drain with several lateral holes, the drain to head toward the papilla. This drain has a double purpose: (1) on the days following the operation the common duct and bladder can be washed with a solution of sodium chlorate or a solution of nitrate of silver, which has proved its value in treating inflammation of the bladder. (2) In the presence of stones which could not be entirely removed, it is possible to carry out the ether treatment described. Around this small drain conducted outward the incision in the bladder is tightened with sutures. Another larger drain, which can be removed on the third day, is securely placed near the region of the anastomosis. Sometimes bile is found to flow out for 2 or 3 days after operation.

At first I used this technique only in cases in which, aside from the finding of stones, no remarkable pathological changes had taken place in the wall of the bladder.

In view of the excellent results obtained in these cases I decided to use the method also in cases in which the gall-bladder walls were badly inflamed and in those in which the bladders were hydropic. Only those in which the wall of the bladders were totally destroyed and those in which abscesses were present were eliminated. In these latter cases mucoclasis[1] should be performed.

In this way I was able to conserve the bladder in the majority of patients brought to my clinic. Of 11 patients thus operated upon I did not have a single mortality. The recovery in all of the patients was excellent, in fact less complications were encountered than after the best cholecystectomy.

First of all, on the third or fourth day after the operation a surprising but common sequel is noted

[1] Pribram. Zentralbl. f. Chir., 1928, No. 13.

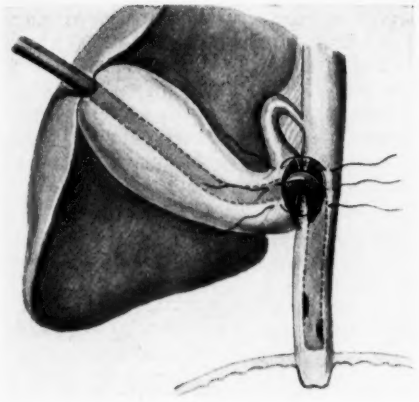

Fig. 18.

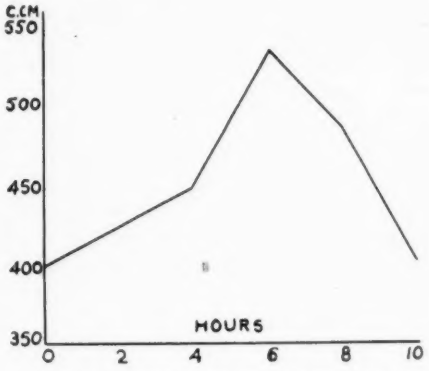

Fig. 19. Normal curve, good reabsorption.

patients develop an appetite which sometimes increases to the point of a pronounced feeling of hunger. It is a well known fact that this does not occur even when patients make the best recovery after cholecystectomy; food tolerance after cholecystectomy is diminished for weeks and months and for good reasons the rule that a strict diet be prescribed is observed. I have often made the interesting observation that cholecystectomized patients complain that all food has the same taste and that the gift for discerning the taste of different foods becomes less pronounced after the loss of the gall bladder.

Quite different is the story of the patient who has been treated with cholecystocholedochostomy: the patient shows not only, as mentioned, an appetite extraordinary for the third or fourth day after operation but in the first week he tolerates food much better than could be expected from his condition before operation.

I have observed patients whose tolerance for food had become so poor during the course of the gall-stone disease that they could not only not tolerate fat but even meat and eggs could not be eaten. On the fourth day after operation, however, these same patients were able to eat food of every kind, a thing they had not been able to do since the beginning of their illness.

I wish particularly to emphasize the food question, the increase in tolerance for food being one of the most interesting and most common sequel after cholecystocholedochostomy. This fact does not seem so extraordinary when we recall our experiments concerning the function of the gall bladder and the activating importance of the bile of the gall bladder.

The number of patients operated upon by this method and the period of observation is too short

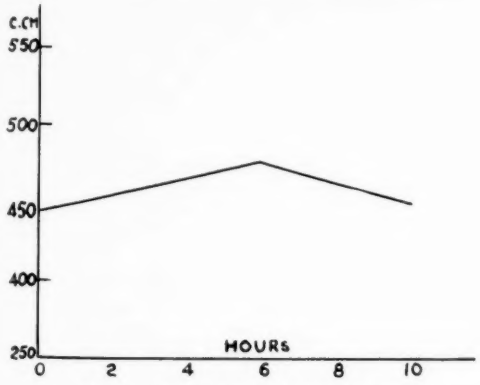

Fig. 20. Curve showing bad reabsorption of fat.

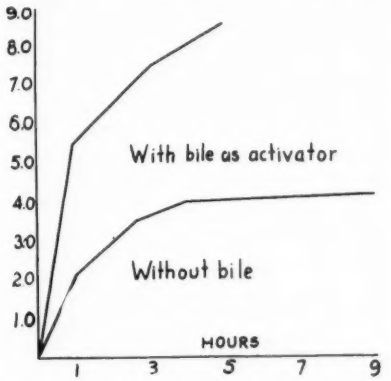

Fig. 21. Effect of activators. Mixture of pancreatic lipase of distinct titre with oil emulsion.

(the first case being under observation for a year) to enable us to form a definite opinion of the value of this new operation. To be able to say something really definite we should have not only thousands of cases but our study should be carried over several years. We must remember that 50 years have elapsed since cholecystectomy came into use and it is only recently (see especially the report of the Congress in 1932 at Vichy concerning the end-results of cholecystectomy), that doubts have been expressed as to the advisability of removing a functionating gall bladder.

At any rate, based on the excellent results I have obtained, I believe that this operation merits further investigation. One fact I believe should be stated: cholecystocholedochostomy seems to be the most logical operation to use in cases in which the gall bladder is in a state of stasis.

One other thing should be mentioned: surgeons and physicians all agree that the chances for favorable results of the operation are best when the patient is operated upon in the early stages of the disease rather than when the disease has progressed. However, the arguments of physicians and surgeons against operation performed in the early stages concern principally (aside from the operative risk) the early removal of the gall bladder and the fact that at times there is a remarkably high percentage of recurrent complications.

If, by operating at an early stage, we are able to avoid recurrences by conserving the gall bladder with its complete function and, more than this, if we can overcome disturbances in function we should be more emphatic in insisting upon the necessity of an early operation.

THE INCIDENCE OF GASTROJEJUNAL ULCER FOLLOWING GASTRO–ENTEROSTOMY[1]

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THE ever perplexing question as to what percentage of patients develop gastrojejunal, or marginal ulcers, following a gastro-enterostomy, creates as much controversy now as when partial gastrectomy was advocated a decade ago to eliminate this serious sequela of a gastro-enterostomy. The incidence of marginal ulcer was found so high in some clinics it was thought that the routine gastro-enterostomy should be discontinued and the more radical procedure, partial gastrectomy, done. In 1925 Lewisohn published a paper in which he studied 68 patients and found 34 per cent of gastrojejunal ulcers in their clinic. His paper brought forth considerable discussion and men in numerous clinics felt that a gastro-enterostomy was rarely followed by a marginal ulcer. A recent paper by Gaither in which he studied 100 cases and found the results most satisfactory, would indicate that there is still considerable difference of opinion as to how frequently gastrojejunal ulcer is seen following gastro-enterostomy.

We feel that the results from gastro-enterostomy in the Gastro-Enterological Clinic of the Fourth Medical and Surgical Division of Bellevue Hospital should be recorded. Our clinic is now over 6 years old and we have had the opportunity to study some cases for a long period, therefore we wish to report the cases of gastro-enterostomies entering the clinic from January 1, 1928 to January 1, 1933. During this period we have admitted 583 cases of peptic ulcer, and of this group 440 cases were unoperated upon at the time of admission which leaves only 143 cases that were operated upon before entering the clinic. Of the 143 patients who had been operated upon before entering the clinic, 90 had been operated upon for chronic ulcers, and 79 of these had had gastro-enterostomies performed. We will consider only the 79 cases having had gastro-enterostomies, and of this group we have encountered 13 patients with gastrojejunal ulcers which is 16.4 per cent of marginal ulcers occurring in the gastro-enterostomies during the 5 year period.

Before going into a detailed discussion of the cases we wish to present it would seem worth while to call attention to the fact that our clinic has been run for the purpose of closely observing patients suffering from peptic ulcer to see what the final results are from the different methods of medical and surgical treatment. During the 5 year period from January, 1928, to January, 1933, 583 patients observed in our clinic made a total of 9,567 visits which would average 16.2 visits per patient for the 5 year period, or 3.2 visits per patient per year. It is important, in drawing conclusions from patients treated for a peptic ulcer, to have frequent observations as to his clinical course, otherwise conclusions are most inaccurate. From the observations in our clinic we feel that a follow-up letter is more misleading than helpful in drawing conclusions in ulcer patients. Also any report based on a single observation, after one to several years have elapsed, following operations, is also misleading. It is known that the symptomatology of a peptic ulcer runs in cycles, and unless there are frequent periods of observation of the clinical course, this periodicity may be lost and the patient seen in the interval will be symptom free and frequently forgets the discomfort he has suffered a few months before. We would like to call attention to the fact that we have carefully selected the patients that have been referred from our clinic for operation, and of the 583 cases, 440 as previously stated, were unoperated upon at the time of being registered in the clinic and of this number we have referred only 33 patients for operation during the first 5 years, which indicates that we have tried to select the patients for operation with the greatest possible care.

To illustrate the seriousness of gastrojejunal ulcer we wish to report a case which came under our observation during 1933 and which is extremely interesting. In this case the gastrojejunal ulcer followed a gastric resection and is not included in our percentage figures, as we are including only those that followed gastro-enterostomy. The case is presented merely to impress the seriousness of a marginal ulcer.

Male, 27 years of age, admitted to the clinic February 16, 1933, having been discharged from the hospital 12 days before, after being operated upon for a perforated gastrojejunal ulcer. The patient first had pain in his stomach in

[1]Read before the American Gastro-Enterological Association on April 30, 1934 Atlantic City, New Jersey.

1928, associated with nausea and vomiting after meals. At the time a diagnosis of duodenal ulcer was made and the patient was placed on a Sippy diet. His condition improved but 6 months later he collapsed on the street and was taken to St. Mark's Hospital with a severe hæmorrhage. The patient was transfused and later operated upon in that institution and a resection of the stomach done, with a Pólya anastomosis for an ulcer of the duodenum. The patient felt well until 2 years later, or in 1930, when he had a severe hæmorrhage from his stomach and was again referred to the same hospital and at this time he was transfused. Following this he felt well, although he had slight abdominal pain until May, 1932, when he had a sudden severe pain which caused him to collapse and he was referred to the Peoples Hospital and operated upon for a perforated ulcer in the jejunum, one inch distal to the anastomosis. The perforation was closed, and the patient made an uneventful recovery and felt well for about 5 months. In January, 1933, however, he began having pain in his abdomen which was fairly severe and on January 30, 1933, he was seized with sudden severe pain in his abdomen and was sent to Bellevue Hospital. The operation revealed at the gastrojejunal anastomosis a perforated ulcer of the jejunum one-half inch from the margin of the anastomosis on the jejunal side and the perforation was about one-quarter of an inch in diameter and surrounded by plastic exudate. The perforation was sutured but due to marked kinking it was necessary for the operating surgeon to do an entero-enterostomy between the proximal and distal loop of the jejunum.

The patient was seen in the clinic 5 times during the early part of 1933 and was last seen on May 31, 1933, when he felt quite well and had been symptom free for 3 weeks. X-ray series were purposely not ordered immediately following his operation due to fear of additional trauma from manipulation at the site of the anastomosis. This patient, of course, illustrates a very dramatic picture of what can happen from a peptic ulcer in spite of the fact he was receiving medical treatment for his ulcer when the first hæmorrhage occurred. For anyone to offer a prognosis on this case would be mere speculation and the case is presented to illustrate the seriousness of gastrojejunal ulcer.

CASE 1. Male, Russian Jew, 38 years of age, admitted to the clinic, July 14, 1928. Before admission to the clinic he was complaining of abdominal pain after meals which would come on 2 to 3 hours after eating and it would bother him at intervals of a few weeks to a few months at a time, although he had been operated upon 3 times for ulcers of his stomach. Patient was first operated upon in 1922 at Beth Israel Hospital, New York City, for a duodenal ulcer. Previous to his operation he had had ulcer symptoms for one year and had had medical treatment for his ulcer without relief of his symptoms and operation was advised. A gastro-enterostomy was performed and the patient was well for 6 months after which he began having severe pain which was similar to that preceding his operation but more severe. He was under medical treatment and very little relief was obtained from his symptoms. X-ray series on December 17, 1925, revealed a duodenal ulcer but otherwise negative. Patient first entered Bellevue Hospital December 16, 1925, and was discharged January 13, 1926. He was operated upon December 30, 1925. At operation the omentum and stomach were found adherent to the anterior abdominal wall with the transverse colon fixed to the site of gastro-enterostomy. The duodenum revealed a healed ulcer one inch distal to the pylorus. The gastro-enterostomy was placed high on the posterior wall of the stomach with a jejunal ulcer one half inch from the stoma on the efferent loop of the jejunum, penetrating into the transverse colon. The ulcer was excised from the jejunum but its base was left attached to the transverse colon, and carbolized and inverted. The gastro-enterostomy anastomosis was disassociated and the stomach wall closed with 2 layers of No. 1 chromic catgut. An end-to-end anastomosis was done in the jejunum No. 1 chromic being used for the closure. Convalescence was uneventful, patient was seen regularly in the follow-up clinic and on March 7, 1926, he had gained 18 pounds in weight but was having an occasional burning sensation after eating but was following his diet regularly. The patient was seen at monthly intervals during April, May, June, July, August, and September, and during all of these visits complained of slight abdominal discomfort but no typical ulcer pain. On his last visit October 3, 1926, he had gained 23 pounds. He failed to return to the follow-up clinic and on September 4, 1927, could not be found at his previous address. He was re-admitted December 17, 1927, complaining of a burning pain in the epigastrium, belching of gas of a few days' duration. X-ray series December 18, 1927, revealed a duodenal ulcer. Patient was again operated upon December 23, 1928. There was found an ulcer in the first portion of the duodenum on the anterior superior surface and marked adhesions in the right upper quadrant but the site of the former gastro-enterostomy was inspected and there was no evidence of obstruction to the jejunal anastomosis. The duodenum was separated from the under surface of the liver and the ulcer was infolded with No. 2 chromic pursestring sutures but not excised. The patient made a rather stormy convalescence, developed pneumonia in the right lower lobe, following which he developed empyema. He was operated upon February 18, 1928, for an empyema of the right chest and the eighth rib in the posterior axillary line was resected. He made an uneventful convalescence and was discharged from the hospital March 9, 1928. After coming under our observation July 14, 1928, patient continued to have abdominal discomfort but returned to the clinic at irregular intervals; although he was instructed to return at weekly intervals he came back at periods of 3, 4, to 6 weeks. He was put on a Sippy diet when he first entered the clinic and given aolin subcutaneously. X-ray series on June 14, 1929, revealed an ulcer of the first portion of the duodenum; no 6 hour gastric retention. In spite of these findings he returned for treatment rather spasmodically and on September 20, 1929, he entered Post-Graduate Hospital and was operated upon for an ulcer of the duodenum. Report from that institution was as follows: "Diagnosis: Pyloric ulcer with obstruction, and marked gastric dilatation. Operation was posterior gastro-enterostomy, although there was a definite mass in the region of the duodenum, which was practically impossible to free due to the denseness of adhesions in that region. Patient was discharged from that institution on October 10, 1929." Since then we have seen him in our clinic November 23, 1929, August 7, 1930, August 21, 1930, November 6, 1930, November 20, 1930, July 9, 1931, and July 16, 1931. During all these visits he stated he felt quite well and was following his diet very regularly, but has had occasional abdominal discomfort but no real pain simulating an ulcer. X-ray series November 12, 1930, revealed an ulcer of the first portion of the duodenum and a gastro-enterostomy with a normal appearing stoma. X-ray series July 13, 1931, revealed a normal, well functioning gastro-enterostomy, with no evidence of a marginal ulcer. He returned to the clinic on November 1, 1933, stating that he had been having severe abdominal pain for 1 month. A gastro-intestinal X-ray series revealed at that time a gastrojejunal ulcer. He returned for treatment for 1 month and felt improved and discontinued.

It can be seen that this patient was most uncooperative but he had 2 gastro-enterostomies per-

formed and each has been followed by a gastrojejunal ulcer.

CASE 2. Male, Italian, aged 24 years, admitted to the clinic January 21, 1928. Patient had been operated upon in Bellevue Hospital in December of 1927 for an ulcer. Abstract from the hospital was as follows: Patient had been having epigastric pain since July, 1927, which was relieved by food, but would return at 1 to 2 week intervals, and then he would be symptom free for an equal length of time. Occasionally he would be awakened at night by epigastric discomfort which was immediately relieved by the taking of food. X-ray series December 19, 1927, revealed an ulcer of the first portion of the duodenum but no 6 hour residue. Operation December 20, 1927, revealed an ulcer in the first portion of the duodenum just distal to the pylorus, with a definite crater in the ulcer but no other intra-abdominal pathology. A posterior gastro-enterostomy was done, No. 1 chromic catgut being used for the anastomosis, and a routine appendectomy. An uneventful convalescence was made and the patient was put on a fourth week Sippy diet on his first visit to the clinic. On March 10, 1928, he complained of some gas in his stomach after eating but felt better than before his operation and on April 25, 1928, he felt well and had no complaints. On June 9, 1928, however, he was complaining of pain in the epigastrium, of a burning nature. X-ray series on June 22, 1928, revealed the presence of a deformity in the first portion of the duodenum, and an irregularity of the stoma with a niche on the jejunal side of the stoma. On June 23, 1928, patient states he had a different pain in his abdomen from that before his operation. It usually started to the left of the umbilicus and goes to the right side, and the pain had been present for about 8 weeks and had gradually become worse. He was advised to reenter the hospital for operation and after 3 weeks of dietary regimen, without improvement, he was re-admitted July 20, 1928, for operation with the following findings: Adhesions were found between the duodenum and anterior abdominal wall and on inspecting the previous gastro-enterostomy there was found an area of induration on the efferent loop which was adherent to the colon. This was separated. There was also a perforation extending partly through the walls of the colon but it did not involve the mucosa. The gastro-enterostomy stoma was disassociated, the ulcer of the jejunum excised, and an end-to-end anastomosis done in the jejunum. The duodenal ulcer was still present and apparently showed no signs of healing, so a partial gastrectomy was done, and an anti-colic anastomosis was made following the Pólya-Balfour technique. Following the operation the patient developed pneumonia and in spite of this made a very smooth convalescence for the first 4 days and then became quite ill and died on July 26, 1928, from a lobar pneumonia.

In reviewing this case one could criticize the operating surgeon for having operated upon the patient without adequate medical treatment. The patient never had any systematic medical management and was also quite young, only 24 years of age. The marginal ulcer developed within 6 months following his original operation and he was re-operated upon 1 month after the diagnosis was made. One could, in view of our present knowledge, question the advisability of operating upon the patient for a marginal ulcer without having given him more prolonged medical treatment for the relief of his symptoms.

CASE 3. Male, Russian Jew, 39 years of age, admitted October 20, 1928, with a history of having been discharged from Bellevue Hospital after an operation for an ulcer of his stomach. Résumé of the hospital record is as follows: Admitted September 19, 1928, discharged October 20, 1928. Past history: Patient had had an appendectomy in 1913 for chronic abdominal pain and his present history was that for the past 5 years he has had epigastric distress with heartburn 3 to 4 hours after eating. These symptoms were rather mild until 1 year ago when the epigastric pain became more severe, and occasionally awakened him at night. He has been under the care of different physicians without relief of symptoms. X-ray series made on September 26, 1928, were negative for an ulcer of the stomach or duodenum, but in spite of his negative X-ray series this patient was advised to have an operation which was done on October 6, 1928. At operation the gall bladder was found to be normal but there was a definite ulcer on the posterior wall of the first portion of the duodenum just beyond the pyloric ring, with stippling of the peritoneum, and an indurated area one-half inch in diameter. Operation consisted of a posterior gastro-enterostomy, without clamps, the anastomosis between the stomach and jejunum being done with No. 1 chromic gut. Routine appendectomy was performed and the abdomen was closed in anatomical layers. On November 24, 1928, about 1 month following his discharge from the hospital, the patient was complaining of pain in his upper abdomen but without definite relation to meals. He was following a fourth week Sippy diet but on December 29 the patient complained that for the past 2 weeks the same pain had been present as before operation. The pain came on before meals and was frequently relieved by food, but although an X-ray series on November 21, 1928, revealed the stoma to be normal he continued to complain of pain. X-ray series February 14, 1929, and May 3, 1929, were both negative for a gastrojejunal ulcer, but, in spite of the negative X-ray findings, the patient continued to complain of pain similar to that preceding his operation. This patient was given different treatments, including aolin, subcutaneously, at weekly intervals over a period of months, without any relief. The treatment was then changed to Saunder's streptococcus vaccine, subcutaneously, with very little improvement and X-rays January 17, 1930, revealed the presence of a jejunal ulcer, with the presence of a niche formation, with localized tenderness at the site of the anastomosis. X-ray films taken September 17, 1930, revealed a small niche present just distal to the stoma on the efferent loop, with a localized tenderness at this site characteristic of a jejunal ulcer. His symptoms persisted and he was put on gastric mucin in May of 1931, having been given all other known treatment without any improvement, in spite of the fact that the patient was very conscientious in following his regimen. X-ray series January 11, 1932, revealed just distal to the site of the anastomosis a small niche on the efferent loop of the jejunum with localized tenderness at this area, characteristic of a jejunal ulcer. His symptoms persisted and he was re-admitted to the hospital August 4, 1932, and discharged August 13, 1932, after 9 days of bed rest, with a strict Sippy regimen. In spite of treatment the symptoms have persisted and X-ray series April 26, 1933, revealed the presence of a small niche in the efferent loop of jejunum near the stoma suggesting the presence of a jejunal ulcer, with localized tenderness over this area. The patient was last seen March 10, 1934, at which time he still complained of some discomfort but if anything he had felt better during the past 4 months than any similar length of time since his operation.

We wish to call attention to the fact that this patient has been carried along under medical

treatment for the past 5 years and if anything he has been better for the past 12 months than any time since his operation, but what the ultimate outcome of this case will be time only can tell.

CASE 4. Male, Russian Jew, age 63 years, admitted April 11, 1929. This patient entered the clinic on a follow-up letter, he having been previously operated upon in 1922. At the time of admission the patient had no complaints referable to his ulcer and he stated that his only complaint was constipation and occasional gas after meals, and if his bowels moved he felt perfectly well and had no complaints whatsoever. The patient had felt well since his operation some 7 years previous. Previous admission: Admitted to Bellevue Hospital October 31, 1922, discharged November 16, 1922. At the time of his admission to the hospital he complained of epigastric discomfort and constipation for 15 years. The abdominal pain came on 3 to 4 hours after eating and the intake of food and bicarbonate of soda relieved his discomfort. In the early years of his disease he had remission of pain for months at a time but for the past year a strict diet and bicarbonate of soda has given him very little relief of his symptoms. X-ray series revealed an obstructive duodenal ulcer with dilatation of his stomach. An operation, November 3, 1922, revealed there was an ulcer of the first portion of the duodenum which was large and indurated; there was also evidence of a peritonitis about the right upper quadrant. A posterior gastro-enterostomy was done, No. 1 chromic gut being used for the anastomosis. No clamps were used. A routine appendectomy was also done. At the time of admission to the clinic April 11, 1929, the patient's complaint was constipation and he was put on a diet for this He was referred for X-ray series and barium enema and on May 24, 1929, gastro-intestinal series revealed a persistent deformity of the inner and outer part of the first portion of the duodenum with normal gastro-enterostomy stoma, and without evidence of a niche or localized tenderness. The barium enema on June 18 reported no organic lesion of the colon. In the early part of June the patient began complaining of slight epigastric discomfort, but in view of the negative X-ray reports this was discounted to a great extent and treatment was continued for his constipation. On August 17, 1929, he complained of quite severe pain in the epigastrium and he continued to complain of this for the next 2 months, although he was put on a fourth week Sippy diet and was given aolin subcutaneously. X-ray series December 13, 1929, revealed a niche just distal to the stoma in the efferent loop of jejunum with localized tenderness. Diagnosis: Jejunal ulcer. X-ray series on February 21, 1930, revealed the presence of a jejunal ulcer with a small 6 hour residue, at the site of the anastomosis. The patient at this time was complaining of severe pain and he had been under the care of one of the internists of the clinic since his admission in April of 1929. March 1, 1930, the patient was turned over to the surgical group by the internist stating that no further relief could be gotten from medical management and operation was advised. At this time he was again put on ambulatory Sippy diet and returned 1 week later stating that he was greatly improved. At this time he was also put on aolin 1 cubic centimeter subcutaneously, and had no complaints until October 9, 1930, when he had a slight epigastric discomfort. This he complained of until November 13, 1930, when his pain again entirely disappeared. X-ray series July 30, 1930, revealed the presence of a deformity of the duodenum characteristic of an ulcer but the jejunal ulcer previously visualized was not seen at this time. Re-examination was advised, and X-rays on August 14, 1930 showed a normal functioning gastro-enterostomy stoma, with no evidence of a niche in or about the stoma. The patient remained perfectly well until December 17, 1931, when he returned, stating that he had slight pain for 2 weeks and X-ray series March 25, 1931, failed to visualize the jejunal ulcer previously reported. X-rays December 14, 1931 revealed an ulcer at the pyloric ring but no 6 hour retention and a normal stoma. At this time the patient was put on Saunder's streptococcus vaccine, intravenously, starting with 50,000 at the first injection and increased 25,000 weekly. On January 14, 1932, the patient was perfectly well, and since January, 1932, the patient has been free from symptoms and was last seen December 27, 1933, when he stated that he had felt perfectly well for the past year and a half. X-ray series done May 2, 1932, revealed the presence of a duodenal deformity with a normal stoma and no evidence of niche formation or localized tenderness could be demonstrated.

It is worth while noting that in this patient his operation was done in November of 1922, and he was symptom free until June of 1929, except for constipation. His X-ray series was negative in May of 1929 for a marginal ulcer but a gastrojejunal ulcer was demonstrated in December of the same year, or 7 years following his gastroenterostomy. It is interesting to note that this patient had been given up by the internist in the clinic as a medical failure, and after giving him another trial with a Sippy regimen his symptoms disappeared in about 6 months after their onset. With the exception of 2 slight flare-ups, one in October of 1930, or 6 months after he had been entirely free from symptoms, and another in December of 1931, after he had again been free from symptoms for a year's time, this patient has been entirely well. From his repeated X-ray examinations it is certain this patient developed a gastrojejunal ulcer and this type of ulcer can run periodicity, as does a peptic ulcer.

CASE 5. Male, American, age 33 years, admitted to the clinic March 29, 1930, complaining of pain in the epigastrium. He had been treated in the medical wards of the hospital for a marginal ulcer from March 8, 1930, to March 29, 1930. A résumé of the hospital records revealed that in 1928 he had been operated upon for a duodenal ulcer and a gastro-enterostomy had been performed in the Greenwich Hospital. Previous to the operation he had had epigastric discomfort after meals for a period of 8 years. Following the operation for a period of 4 months he had felt greatly improved but then the pain had returned and for 4 months before admission to Bellevue Hospital he had had tarry stools and had vomited blood for a 5 day period. X-ray series March 11, 1930, revealed the presence of an ulcer in the efferent loop of the jejunum, just distal to the site of the stoma with the duodenum deformed and a small 6 hour gastric residue present. He was placed on a Sippy regimen and referred direct to the clinic on leaving the hospital. At the time he entered the clinic he was placed on Saunder's streptococcus vaccine, intravenously, 25,000 bacteria being administered at the first injection and the amount increased 5,000 a week, so as to avoid any reaction. Immediate relief of pain was attained after entering the clinic and there were no complaints until August 7, 1930, when he complained of some abdominal discomfort which lasted until September

11, when it entirely disappeared. X-ray series August 13, 1930, revealed a small niche distal to the stoma in the jejunum, with localized tenderness at this area, characteristic of a jejunal ulcer. The patient had no further complaints until January 15, 1931, when he had some epigastric discomfort which he complained of until March 5, 1931, when it disappeared, after which time he was symptom free for 10 weeks. X-ray series March 2, 1931, revealed a deformed stoma with a niche in the jejunum, distal to the site of the anastomosis which was exquisitely tender to palpation. Diagnosis: Jejunal ulcer. At this time the patient was receiving Saunder's vaccine, intravenously, and was returning weekly for treatment until May 21, 1931, when he had a return of his abdominal pain. Then he was given gastric mucin and on June 11, 1931, he was greatly improved and had very little discomfort. Two weeks later he was symptom free and was on an unrestricted diet. Since that time the patient has been practically symptom free, except for 2 flare-ups of symptoms lasting for 1 to 2 weeks. He was last seen January 24, 1934, at which time he was symptom free and had been so for approximately 1 year. X-ray series March 21, 1932, revealed the following: Folding of greater curvature of the stomach on either side of the stoma, with diminution of the normal jejunal marking in the distal loop of intestine but no niche or localized tenderness present. The evidence indicates a gastroduodenitis but the presence of an ulcer in association with it cannot be substantiated on the basis of the roentgenological evidence at this time.

This patient is of considerable interest as there seems to be very little question about the diagnosis of a gastrojejunal ulcer and with varying types of medical treatment this patient has been symptomatically cured for approximately 1½ years, and this, of course, is important when one is usually taught that marginal ulcers do not respond to conservative treatment.

CASE 6. Male, Irish American, 36 years of age, admitted November 3, 1928, complaining of abdominal pain and having been discharged from the medical service of the hospital the day of admission to the clinic. Résumé of the hospital records was as follows: Admitted October 15, 1928, discharged November 3, 1928. Complaint: Pain in epigastrium coming on 1 to 2 hours after meals for the past 5 years, and it awakens him from his sleep. Occasionally he vomits but usually bicarbonate of soda, or food, relieves the pain. During the past year his pain has been getting more severe and more persistent and he has had very little freedom from his discomfort. X-ray series October 18, 1928, revealed a filling defect in the inner and outer part of the duodenum, characteristic of a duodenal ulcer. A Sippy diet was followed while he was in the hospital. The patient stated that 5 years before he was X-rayed and told he had a duodenal ulcer and was treated at that time for the ulcer with temporary improvement. He made only one visit to the clinic and was admitted to the hospital as an emergency case February 24, 1929, with a history of having been well since his discharge from the hospital until one week before his admission when he began having pain in his epigastrium. About 6 hours before his admission he felt a severe pain in his upper abdomen which caused him to collapse in the street, due to the intensity, and was brought to the hospital in a taxi. A diagnosis of perforated duodenal ulcer was made, and the patient operated upon immediately. Operation revealed a duodenal ulcer in the anterior superior portion of the duodenum which had perforated. The indurated area was excised and the duodenum closed with No. 1 chromic gut, 3 interrupted layers of sutures being used. An uneventful convalescence was made and the patient was discharged from the hospital March 15, 1929, and re-admitted to the clinic March 16, 1929. He was seen regularly in the clinic until August 10, 1929, and at the time of this visit he was complaining of pain in the epigastrium which he had for the past 2 weeks. Although he did not return to the clinic following this visit he was re-admitted to the hospital January 6, 1930, and discharged January 27, 1930. X-ray series January 8, 1930 revealed a persistent filling defect of the inner and outer borders of the duodenum with a 6 hour gastric residue of one-third of the meal. Operation on January 10, 1930 revealed the anterior superior portion of the duodenum an indurated area which had stippling over it and a partial obstruction of the pyloric ring, with slight dilatation of the stomach. A posterior gastro-enterostomy was done with No. 1 chromic sutures for the anastomosis, without clamps. The abdomen was closed in anatomical layers. The patient returned to the clinic February 1, 1930, at which time he was symptom free and his abdominal incision entirely healed, but he made only 2 visits and was last seen March 8, 1930, when he was perfectly well. He was not seen again until August 13, 1931, when he had no pain or complaints but returned March 2, 1933, complaining of severe abdominal pain for the past 2 days. X-ray series March 10, 1933, revealed tenderness over stoma, with a niche formation at the site of stoma. The patient was then put on a first week Sippy diet, with powders, and his symptoms improved. On May 4, 1933, he had gained 12 pounds and was free from complaints. On his last visit November 14, 1933, he was symptom free.

One can see that this patient was a rather uncooperative individual and no matter what the type of treatment was used on this patient a poor result could be expected, as he usually did not return for treatment until he had a return of symptoms, and he also used alcohol and tobacco to excess.

CASE 7. Male, Irish American, age 35 years, admitted to the clinic February 18, 1932, complaining of epigastric discomfort which was severe. He had been operated upon in 1924 for an ulcer of his stomach. Résumé of previous admissions was as follows: Patient admitted to Bellevue Hospital May 27, 1924, discharged June 15, 1924. Complaint: Attacks of pain in epigastrium since 1920 which would come on about 30 minutes to 3 hours after eating and was relieved by food. X-ray series May 29, 1929, revealed a duodenal ulcer but no 6 hour retention. Operation June 3, 1924: An ulcer on the anterior superior portion of the duodenum just distal to the pylorus which was penetrating through the entire coats of the duodenum but the gall bladder was normal. A posterior no-loop gastro-enterostomy was done without clamps, No. 1 chromic gut being used for the anastomosis. The ulcer was inverted by several interrupted mattress sutures and a routine appendectomy was done. At the time of entering the clinic February 18, 1932, the patient had been entirely well until 3 weeks before his admission when he began having epigastric pain which was more severe than that he had previous to his operation. X-rays on February 19, 1932, revealed an ulcer in the first portion of the duodenum but the patient was requested to return for a more careful study of the gastro-enterostomy stoma. Re-examination March 7, 1932, revealed a duodenal ulcer and a gastro-enterostomy functioning normally, but no niche suggestive of an ulcer in this region was found. The patient's pain was so severe

that he was advised to enter the hospital for bed rest. He remained in the hospital for bed rest from March 8 to March 13. His symptoms subsided while in bed and on a Sippy diet and he asked to leave the hospital. He returned to the clinic for treatment and his pain became so severe within 2 weeks that he was forced to return to the hospital and was operated upon. In spite of negative X-ray findings a diagnosis of gastrojejunal ulcer was made and he was operated upon March 25, 1932. The abdomen was opened and the duodenum was found mobile but both palpation and inspection were negative for an ulcer. On inspecting the stoma from the previous gastro-enterostomy it was found to be patent and an ulcer was found on the posterior wall of the stomach near the anastomosis. The ulcer was about the size of a five cent piece, and penetrating from the posterior wall of the stomach into the pancreas. As it was not possible to disassociate the anastomosis and excise the ulcer, the only method of approach was a partial gastrectomy. The ulcer in the stomach was freed from the pancreas with difficulty and the jejunum at the site of the anastomosis was excised, and an end-to-end anastomosis done. An anticolic anastomosis was done between the jejunum and stomach, using the proximal loop to the greater curvature, and distal to the lesser, as it caused less rotation of the intestine by this approach, and No. 1 chromic sutures used. Then an entero-enterostomy was done between the proximal and distal loops of the jejunum.

The penetration of the ulcer into the pancreas necessitated a subtotal gastrectomy, as the ulcer could not have been excised by any other surgical procedure. The patient made an uneventful convalescence following the operation and has been seen in the clinic at frequent intervals and was last seen November 15, 1933, at which time he was perfectly well and had no complaints. X-ray examination of the gastro-intestinal tract November 3, 1933, revealed the presence of a gastric resection but no evidence of a marginal ulcer.

It is worth-while noting that this patient went for 7 years and 8 months entirely free from symptoms when his symptoms returned which were more severe than those for which he was operated upon. In spite of 2 negative X-ray series his pain was so excruciating that the diagnosis of gastrojejunal ulcer was made and the patient advised to have an operation. This patient illustrates that a marginal ulcer can occur at long intervals following gastro-enterostomy, and that in spite of negative X-rays one can have such a complication.

CASE 8. Male, Irish American, 39 years of age, admitted to the clinic December 18, 1930, complaining of pain in the small of his back and epigastrium, with a history of having had stomach pain for the past 10 to 12 years. He had been operated upon in the Jewish Hospital, Brooklyn, only 6 months previous to admission for a perforated ulcer. Five years previous to that he had been operated upon in the Jersey City Hospital, an exploratory laporotomy and appendectomy having been done. X-ray series December 29, 1930, revealed a persistent deformity of the outer border of the first portion of the duodenum, characteristic of an ulcer, with a gastro-enterostomy stoma somewhat diminished, with only a small amount of barium going through it. Report from the Jersey City Hospital stated that the patient entered March 22, 1926, discharged April 21, 1926. X-ray series revealed irregular duodenum, otherwise negative, and he was operated upon April 7, an abdominal exploration revealing that the gall bladder, stomach and duodenum were normal, but an appendectomy was done. Patient was admitted to the Jewish Hospital, Brooklyn, March 14, 1930, discharged March 28, 1930. A few hours previous to admission he was seized with sudden pain in the epigastrium and taken to the hospital as an emergency case and operated upon the same day. At this time an old indurated pyloric ulcer was found which had perforated into the pancreas. Operation consisted of closure of the ulcer and a posterior gastro-enterostomy. The patient had relief from his discomfort for only a few weeks. For the past 4 months he has had persistent abdominal pain which is occasionally relieved by food. Saunder's vaccine 0.2 cubic centimeters was given subcutaneously, and this treatment was continued at weekly intervals. On January 15, 1931, he was on a fourth week Sippy diet and was feeling well and had no complaints. He failed to return regularly to the clinic, but on July 30, 1931, he had no complaints and had been symptom free since January. On August 13, the patient complained of severe pain in the epigastrium, and at this time he was advised to take gastric mucin and a second week Sippy diet. Gastric mucin caused nausea and vomiting and he discontinued it. An X-ray series on September 14, 1931, revealed a deformity of the duodenum characteristic of a duodenal ulcer with the gastro-enterostomy functioning normally. However, he continued to have severe abdominal pain and in spite of a strict Sippy regimen and powders he obtained no relief. On October 22, 1931, he was still having severe pain but discontinued treatment and went to a private physician. He returned on September 9, 1932, still complaining of severe pain and was advised to enter the hospital for operation. X-ray series September 4, 1932, revealed a duodenal deformity, stoma normal, and no evidence of a marginal ulcer. Because of the severe pain and prolonged medical treatment, however, clinical diagnosis of gastro-jejunal ulcer was made and operation advised. Operation September 9, 1932: When the abdomen was opened numerous adhesions were found and separated, also a large marginal ulcer on the jejunal side of the anastomosis which had perforated into the pancreas. Exploration of the pylorus failed to reveal any evidence of a duodenal lesion. The stoma was disassociated and the stomach was closed with 3 layers of interrupted No. 1 chromic gut. It was necessary to resect 8 inches of jejunum and to excise the ulcer from the pancreas, and an end-to-end anastomosis to the jejunum was done with No. 1 chromic gut, 3 layers of sutures being used. Patient made an uneventful convalescence and has been seen regularly in the clinic and was last seen November 12, 1933, when he had no pain or complaints referable to his abdomen.

This patient illustrates 3 interesting points: First, he had a duodenal ulcer and during an abdominal exploration the operating surgeon failed to find the lesion which is not an infrequent occurrence. Second, the patient had an acute perforated duodenal ulcer and a gastro-enterostomy was done, which has been advocated in some clinics in acute perforations. In spite of this he developed a marginal ulcer immediately upon his discharge. Third, the X-ray series in this case were all negative, and the clinical diagnosis of jejunal ulcer was made in spite of the negative X-ray findings.

CASE 9. Male, Irish American, age 32 years, admitted to the clinic March 17, 1932, complaining of abdominal pain. He had been operated upon twice for ulcers of his stomach. Patient states that he had had pain in the pit of his stomach since a small child which was relieved by food. It was considered hunger pain until the age of 16 when it became quite severe. He was treated for an ulcer from the age of 16 to 25 but the pain became gradually worse. X-rays in 1918 revealed a duodenal ulcer and as the pain became gradually worse he was operated upon in the Brooklyn Hospital in 1925 and a gastro-enterostomy was done, following which he was free from symptoms for a period of 3 years when in 1928 the pain returned. In that year he was treated in the Kings County Hospital, Brooklyn, for 23 days on a milk diet and powders, following which he was symptom free for about 5 months. In April, 1929, his pain was severe and he went to the Mayo Clinic and was re-operated upon. The report from there revealed a perforating gastrojejunal ulcer with the major portion of the lesion being in the stomach, and perforating into the colon, with a duodenal ulcer on the posterior wall perforating into the pancreas. The operative procedure consisted of disconnecting the gastro-enterostomy, resecting the jejunum with an end-to-end anastomosis, and a resection of the stomach, one-half of the stomach being removed and a Pólya anastomosis being done. Following this operation the patient was free from symptoms until October, 1930, when he had a recurrence of pain and since then he has continued to have recurrent attacks of epigastric pain. X-ray series February 18, 1932, revealed a partial gastrectomy with a functioning stoma, without localized tenderness, or obstructive signs. The patient made only 2 visits to the clinic when on October 6, 1932, he came in complaining of severe abdominal pain with a loss of 4 pounds in weight. X-ray series October 14, 1932, revealed a jejunal ulcer visualized fluoroscopically, but the same was not seen on the plates. October 27, 1932, patient complained of having had a hæmorrhage, with tarry stools, and was in bed for 10 days. On November 3 the hæmorrhage had stopped and he was feeling well. Since then the patient has continued to have attacks of pain every 4 to 6 weeks which may last for 1 to 3 weeks and are very severe. The patient follows a rather strict regimen with powders for the relief of pain. X-ray series April 17, 1933, revealed the presence of a partial gastrectomy and a niche, with tenderness to palpation just distal to the site of anastomosis. Re-examination was requested in one month. The patient has not returned to the clinic since April 20, 1933.

This case is of interest as the patient had symptoms characteristic of an ulcer from early childhood and he was operated upon at the age of 25 and was symptom free for 3 years. He then developed recurrent symptoms and one year later was re-operated upon for a gastrojejunal ulcer. Following the gastric resection for the gastrojejunal ulcer the patient was well for 1½ years and then developed symptoms of a second jejunal ulcer. We have quite conclusive roentgenological proof that this patient is at the present time suffering from a second gastrojejunal ulcer following a gastric resection for the first marginal ulcer.

CASE 10. Male, Austrian Jew, 54 years of age, admitted to the clinic December 11, 1930, complaining of severe epigastric pain for 3 months. The patient had been operated upon in April, 1920, for an ulcer of his duodenum in Bellevue Hospital and the records revealed a gastro-enterostomy was done. Following the operation he had been perfectly well and remained so until 1927 when he had a few symptoms but they cleared up immediately and until 3 months ago he had no real abdominal pain since his operation 10½ years previously. X-ray series November 26, 1930, revealed an ulcer of the first portion of the duodenum and a normal gastro-enterostomy stoma. He was placed on a Sippy diet and his symptoms subsided within a few weeks. On January 27, 1931, he was entirely symptom free and had been so for a period of 10 days. He was not seen between January and July 16, 1931, when he returned complaining of pain in his epigastrium for 3 to 4 weeks. At this time he was placed on Saunder's vaccine 10,000 intravenously, which he received at weekly intervals, increasing the bacteria 10,000 per week. X-ray series August 11, 1931, showed a deformity of the first portion of the duodenum, characteristic of a duodenal ulcer but there was no evidence of a marginal ulcer. From July until November the patient returned at weekly intervals and was following a strict Sippy diet in addition to Saunder's vaccine which was given for 8 weeks without benefit, and then gastric mucin was given for 6 weeks without any relief. In view of his persistent pain he was advised to enter the hospital and was operated upon for a gastrojejunal ulcer, in spite of the negative X-ray series. He was admitted to the hospital November 11, 1931, and was operated upon November 20, 1931. An ulcer was found on the posterior portion of the duodenum which was not adherent to the pancreas. Inspection of the posterior wall of the stomach revealed a large marginal ulcer with the transverse colon slightly adherent over the ulcer. The adhesions were freed but the walls had not been completely perforated. The defect was then closed. The anastomosis dissociated and the jejunum was closed in layers with No. 1 chromic gut, but it was not necessary to resect the jejunum. The stomach was also closed with No. 1 chromic gut. A chronic cholecystitis was found but there were no stones. Cholecystectomy was performed. In view of the poor condition of the patient it was thought inadvisable to do any further surgery on the stomach, although there was a definite ulcer in the duodenum. Since the operation the patient has returned regularly to the clinic and has been improved but continues to have epigastric distress. X-ray series October 17, 1932, revealed an ulcer of the first portion of the duodenum but no 6 hour gastric retention. X-ray series August 4, 1933, revealed a deformity and tenderness over the duodenum but no obstruction or gastric residue. The patient was last seen October 5, 1933, at which time he complained of epigastric distress and pain at intervals but the pains were much less severe than before his operation.

In this case the patient went symptom free for 10½ years after a gastro-enterostomy and then developed severe epigastric pain. In spite of 2 negative X-ray series and systematic medical regimen the symptoms persisted and the patient was operated upon for a marginal ulcer. The history of this case proves that a long follow-up is necessary and too much reliance cannot be placed on X-ray findings.

CASE 11. Female, German, age 47 years, admitted to the clinic April 24, 1930, having been discharged from the hospital on April 1, 1930. At the time of admission to the hospital February 14, 1930, she complained of pain in the right upper quadrant of 3 weeks' duration and for 2 weeks it has been getting more severe. She had been operated

upon 5 years before admission in Germany for a gall-bladder disease and her impression was that the gall bladder had been removed at the time. X-ray series February 24, 1930, revealed the duodenum diminished in size but apparently normal, with a 6 hour residue of two-thirds of the motor meal. Operation February 26, 1930, revealed a normal gall bladder but in the second portion of the duodenum there was an area of induration on the posterior surface which was definitely adherent to the pancreas. A posterior gastro-enterostomy was done, No. 1 chromic gut being used for the anastomosis. The patient developed a jejunal fistula which discharged for several weeks but the wound healed and the patient was discharged from the hospital April 1, 1930. She was symptom free following the operation and on September 3, 1930, X-ray series revealed the stoma normal but the duodenal bulb could not be visualized. On November 1, the patient complained of pain in the region of her scar and examination revealed a localized abscess in the incision. She was admitted to the hospital for incision and drainage of the abscess. While in the hospital she complained of epigastric pain similar to that which she had previous to operation but more severe. On December 24, 1930, X-ray series revealed gastro-enterostomy stoma functioning but a small niche formation at the site of stoma with tenderness over it, characteristic of a gastrojejunal ulcer. The patient was discharged from the hospital January 5, 1931, and she returned to the clinic February 5, 1931 complaining of pain in back and upper abdomen. She continued to have abdominal pain, although she was on a fourth week Sippy diet and Saunder's vaccine, intravenously, beginning with 10,000 bacteria and increasing by the same quantity each week. October 1, 1931, the patient had a second abscess in the abdominal scar and was re-admitted for incision and drainage of abscess. She remained in the hospital 3 days and since her discharge has not returned to the clinic for further treatment.

This patient developed a gastrojejunal ulcer within 9 months from the date of original operation.

CASE 12. Male, German American, aged 36 years, was admitted to the clinic May 28, 1931, complaining of pain in upper abdomen. He had been operated upon for an ulcer of the stomach. Patient stated that following the operation he was well for 2 years and 9 months, but since October of 1930 he has had abdominal discomfort similar to that he had previous to his operation but more severe. In January of 1928 he was operated upon in the Wyckoff Heights Hospital, Brooklyn, and at the time he was operated upon it was for a gall-bladder disease, an ulcer being discovered at the time of operation. Operation consisted of a posterior gastro-enterostomy for a duodenal ulcer, cholecystectomy, and appendectomy. Following this operation the patient was entirely well for 2 years and 9 months after which period he began having epigastric distress similar to that previous to his operation. X-ray series May 26, 1931, revealed gastro-enterostomy stoma with a niche at the junction of the efferent loop of the jejunum, and the duodenum slightly deformed with a gastric retention of one-fifth of the motor meal at the end of 6 hours. Diagnosis: Gastrojejunal ulcer.

At the time of entering the clinic the patient was suffering from very severe abdominal pain and he was put on gastric mucin which treatment he followed regularly. September 15, 1931, his weight was 163 pounds, or a gain of 10 pounds. Since May he has been entirely free of symptoms but X-ray series November 5, 1931, revealed the presence of a persistent duodenal deformity with the structure and function of the stoma normal. The patient has remained well since this period with very occasional flare-up of symptoms of 1 to 2 days' duration, about every 3 to 4 months. X-ray series March 14, 1932, revealed the structure and function of the stoma normal and no 6 hour retention. X-ray series September 1, 1932, revealed 10 per cent residue at the end of 6 hours, deformity of bulb characteristic of a duodenal ulcer, and the jejunum at the site of anastomosis markedly stenosed and deformed with a single speck of barium in the region of the stoma, due probably to a niche at the stoma. January 5, 1932, the patient was complaining of severe abdominal pain and again on January 12, but he did not return to the clinic. A home follow-up on April 26, 1933, revealed that the patient had collapsed in the street and had been operated upon in the Wykcoff Heights Hospital, Brooklyn, as an emergency case, presumably for a ruptured ulcer. Requests to that institution for a summary of their findings have not been answered.

This patient illustrates a marginal ulcer that unquestionably received symptomatic and X-ray evidence of healing, although his symptoms returned and there was positive X-ray evidence that his marginal ulcer had returned. Presumably the ulcer perforated necessitating an emergency operation. This case bears out a clinical observation that marginal ulcers will show periodicity the same as do any type of peptic ulcer whether it be gastric or duodenal.

CASE 13. Male, Scotch American, 45 years of age, admitted to the clinic on January 14, 1928, with a history of having been operated upon in June, 1926, for a perforated duodenal ulcer. At that time a Horsley pyloroplasty was done and he was symptom free for about 1 year when he began having discomfort after eating and was unable to eat large quantities without vomiting. Patient was re-operated upon October 14, 1927, for a pyloric obstruction and at the time of operation he had an organic stenosis of the pylorus. A posterior gastro-enterostomy was done with No. 1 chromic sutures for the anastomosis. An uneventful convalescence was made following the operation. At the time of his first visit to the clinic in January, 1928, he was symptom free and had been since his operation in October of 1927. The patient had had symptoms for 10 years previous to the perforation in 1926 and the pain before the perforation came on about 2 hours before meals and lasted for 1 to 2 months at a time, when it would disappear and he would feel perfectly comfortable for a period of 3 to 4 months. The patient remained in the clinic and returned regularly at monthly intervals through 1928 and 1929 and he was symptom free until August 10, 1929, when he complained of abdominal discomfort, with occasional vomiting. Gastro-intestinal X-ray series done May 31, 1929, revealed the gastro-enterostomy stoma normal and no 6 hour retention. After a restricted diet he became symptom free in 1 month and remained well until September, 1933, when he complained of severe abdominal pain which he had had for 2 weeks.

The patient's pain was so severe that he was admitted to the hospital September 26, 1933, and remained until October 27, 1933. A gastro-intestinal series was done on October 6, and again on October 25, which revealed a niche in the jejunum just distal to the site of the anastomosis and a diagnosis of gastrojejunal ulcer was made. The patient left the hospital symptom free on October 27, and has been seen in the clinic four times since and he has remained symptom free.

This patient illustrates a gastrojejunal ulcer which occurred 6 years after a gastro-enterostomy which was performed for a true organic stenosis, following a plastic operation for a perforated duodenal ulcer. Both the first and second operations were done by one of us (J. W. H.). The patient was a most co-operative individual and in spite of the absolute indication for a gastro-enterostomy he developed a gastrojejunal ulcer which at the present time is under control with a dietary regimen.

SUMMARY

The cases here presented are reported in detail so as to give a complete clinical picture of each. Of 13 patients 5 were operated upon in hospitals in or around New York and 8 were operated upon at Bellevue Hospital; no 2 patients were operated upon by the same surgeon. From the review of our cases we feel that any conclusions drawn as to the percentage of gastrojejunal ulcers developing after gastro-enterostomy is most inaccurate unless the patient has been followed for a 10 year period, and also seen at frequent intervals, with repeated X-ray examinations. A follow-up letter in stomach cases we believe is not only inaccurate but misleading and instead of being a help usually presents false information. It is seen that 3 of our patients who came to operation developed symptoms of a marginal ulcer after 7 years, one 10½ years following gastro-enterostomy.

When one realizes that the great majority of our patients have been followed less than 5 years and that in 79 gastro-enterostomies we have encountered 13 gastrojejunal ulcers, or 16.4 per cent, and of the 13 cases 3 occurred after 7 years, it would seem that a 10 year follow-up is necessary in drawing conclusions as to the percentage of gastrojejunal ulcers.

It is important to emphasize that, to a great extent, gastrojejunal ulcers run the same course as do peptic ulcers, that is the patients have pain with periodicity, and freedom from symptoms for intervals of weeks or months—one reason why the flare-ups that are occasionally seen in patients after operation are passed over lightly if X-ray examinations have not been taken. Our cases have also illustrated that too much dependence cannot be placed upon a negative gastro-intestinal examination, for patients frequently will have a marginal ulcer in spite of several negative gastro-intestinal series.

Medical treatment should be tried for as long a period as the patient progresses satisfactorily because marginal ulcers will get symptomatic relief from conservative treatment the same as will any peptic ulcer. If the patient continues to have severe pain under medical treatment it usually means the marginal ulcer is perforating into some adjacent viscus, the pancreas and transverse colon being the organs most usually involved. For that reason it is best to submit a patient with a gastrojejunal ulcer suffering severe pain to a second operation, rather than to continue medical treatment, if the pain is not relieved or improved rather promptly under conservative treatment.

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MELANO–EPITHELIOMA AND HÆMANGIO–ENDOTHELIOMA OF THE ANUS

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THE four cases here reported are considered in a group because of the common anatomical situation of the growths, the apparent similarity of the symptoms and signs, and the rarity of occurrence of such cases. Reporting them in this manner may serve to emphasize the consideration of several important factors in the diagnosis and treatment of anorectal lesions.

One who reads the literature concerning anorectal pathology scarcely can fail to be confused by the considerable variation in the anatomical limitations given for the anal canal. For purposes of this paper the anal orifice will be considered to be that part of the anorectal canal that is distal to the dentate margin.

REPORT OF CASES

CASE 1. A man, aged 54 years, registered at the Mayo Clinic August 16, 1929. His chief complaint was of painful defæcation of 3 weeks' duration. He also complained of a constant desire to defæcate. His appetite had remained normal and he had not lost appreciable weight. He denied having had previous rectal trouble.

His pulse rate and temperature were normal and nothing abnormal was revealed by examination of his blood and urine. Sigmoidoscopic examination (24 centimeters) revealed a firm, irregular mass, measuring 2 by 2 centimeters, involving the anterior anal wall. On the surface of this mass was some ulceration, and bleeding occurred readily. There was some spotty pigmentation in the skin of the anterior anal margin. A tentative diagnosis of melano-epithelioma was made (Fig. 1).

August 19, 1929, the involved region was widely excised under sacral anæsthesia. Following the operation, radium was applied locally and over the groins and this application was repeated in June, 1930, when the patient returned for examination and further treatment. He had gained weight and strength for 6 months after his first treatment, but, when he returned, some palpable lymph nodes were discovered in his groin. He returned again October 27, 1930, at which time he complained of some abdominal pain, and also of some pain in his thorax. Roentgenographic examination of the thorax revealed metastasis. The man died May 3, 1931, at his home and postmortem examination was not made.

CASE 2. A man, aged 39 years, registered at the clinic December 26, 1933. He stated that he had been troubled with rectal discomfort for 4 years. This consisted chiefly of pain during and after movement of the bowels. He had also been distressed by severe constipation, which had been marked during the preceding 4 years. Recently, however, he had obtained relief by taking mineral oil. Six years before his registration he had had some trouble that suggested the possibility of renal colic. He had received local treatment for an anal fissure 4 years before and, since that time, he had also received frequent treatment for "piles." Two months before his registration at the clinic a physician had removed some "proud flesh."

His pulse rate, temperature, and blood pressure were normal. Examination of the urine and blood failed to reveal any abnormalities. Roentgenographic examination of the thorax, kidneys, ureters, bladder, and colon all failed to reveal the presence of any pathological processes. His tonsils were slightly infected and some tenderness was discovered in the right subcostal region and the right lower abdominal quadrant.

Sigmoidoscopic examination disclosed some scars in the anal canal and some external hæmorrhoids. In December, 1933, the anus was dilated, but dilation was limited because of the scars that were present. The external hæmorrhoids were excised. A scar in the anterior median line also was incised and the overhanging edges were removed. There was a considerable amount of scar tissue in the external hæmorrhoidal portion, especially on the right side. Microscopic examination revealed hæmorrhoidal tissue with an associated early melano-epithelioma (Fig. 2).

CASE 3. A housewife, aged 69 years, registered at the Mayo Clinic August 12, 1926. She complained of tenesmus, but sigmoidoscopic examination did not reveal any lesion. The diagnoses were pyorrhœa, septic tonsils, and arteriosclerosis. The woman returned to the clinic in 1933. At that time she stated that she had noticed some painless swelling at the anus. The protruding tissue could be replaced but soon returned to its original situation. Four years previously she had been told that she had some hæmorrhoids but these had not caused difficulty nor had there been any change in the anal condition except for the appearance of the hæmorrhoids.

The pulse rate was 100 beats per minute, the temperature normal, the blood pressure in millimeters of mercury 186 systolic and 80 diastolic, and the urine normal. Examination of the blood revealed that leucocytes numbered 12,700 per cubic millimeter of blood on one occasion, and 11,900 on another, but no abnormalities were observed in the differential leucocyte count. Roentgenographic examination of the thorax disclosed some localized fibrosis in the first intercostal space. The edge of the liver was tender. Sigmoidoscopic examination (24 centimeters) revealed a small, firm nodule at the anal edge in the anterior median line. It was thought that this might be a thrombotic external hæmorrhoid, but in view of the fact that there had been no pain and no tendency for the nodule to subside, operation was advised.

In July, 1933, the nodule was excised, the anus dilated, and 3 cubic centimeters of a 5 per cent solution of quinine and urea were injected into some small internal hæmorrhoids. Microscopic examination of the tissue revealed a hæmangio-endothelioma graded 1 (Fig. 3). Convalescence was uneventful, and before the patient was dismissed from our care, August 5, 1933, 330 milligram hours of radium were applied to the healing wound. The patient was requested to return for re-examination November 13, 1933.

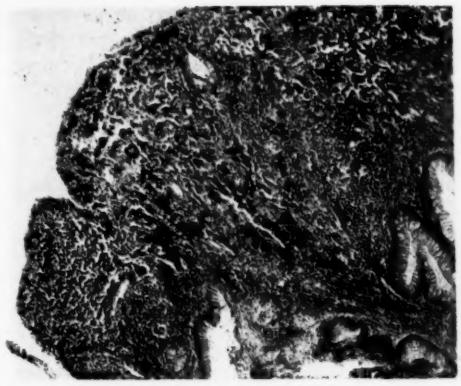

Fig. 1. Melano-epithelioma. Diffuse cellular growth and collections of melanin. (Case 1.)

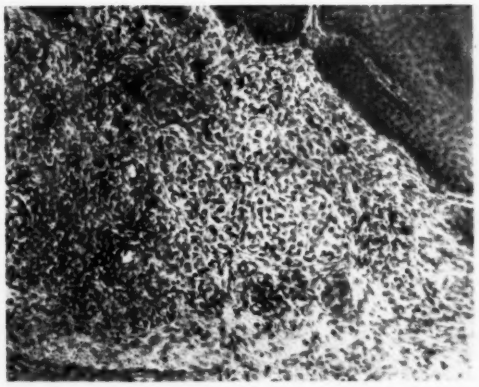

Fig. 2. Melano-epithelioma. Alveolar formation; also a few collections of melanin. (Case 2.)

She did this, and at that time there was no evidence of recurrence or extension of the process.

Case 4. A housewife, aged 48 years, registered at the clinic January 1, 1932. Her chief complaints were of discomfort in the upper right abdominal quadrant and of a sinus at the lower end of the spine. The patient gave a very long and detailed history of attacks of abdominal discomfort, nausea, and vomiting aggravated by ingestion of fried or greasy foods, but denied having had jaundice at any time. The sinus mentioned had been present intermittently for 12 years.

The pulse rate, temperature, and blood pressure were normal. Laboratory examinations of the urine revealed a slight trace of albumin. Examination of the blood, including a platelet count, and estimation of the bleeding and coagulation time, did not disclose any variation from normal. Roentgenographic examination revealed that the heart was moderately enlarged, but there were no demonstrable lesions in the stomach or colon.

The heart sounds were distant, and the abdomen was scarred from previous surgical procedures which included removal of an ovarian cyst from the left side in 1912, removal of a cyst from the right side in 1914, suspension of the uterus in 1914, an operation to relieve adhesions because of abdominal pain in 1915, and excision or section of "a nerve on the right side" for the relief of abdominal pain in 1916.

Sigmoidoscopic examination, limited to 20 centimeters because of the presence of sharp angulation, disclosed the presence of moderately extensive internal and external hæmorrhoids and a draining sinus in the posterior median line, 3 centimeters from the anal edge. Operation was advised. The patient returned to her home and remained there until March, at which time she reappeared at the clinic for surgical attention. The fistula was repaired and the hæmorrhoids were ligated and excised. The pathologist reported that the specimen removed was inflammatory cavernous hæmangio-endotheliomatous tissue, with foreign body giant cells (Fig. 4).

Her convalescence was uneventful and there has been no evidence of recurrence of the condition up to the present time.

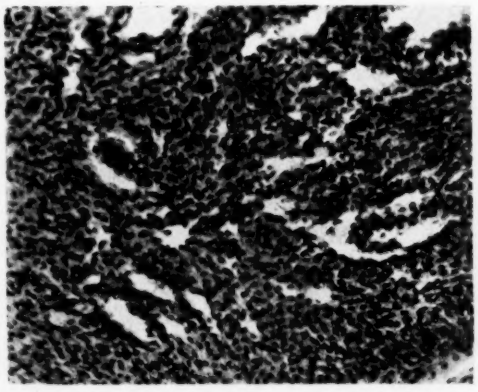

Fig. 3. Hæmangio-endothelioma, graded 1. The endothelial cells to a large extent have differentiated into capillaries. (Case 3.)

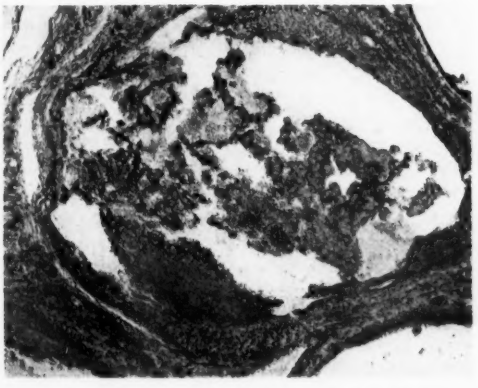

Fig. 4. Hæmangio-endothelioma graded 1. A cavernous area made up of erythrocytes and a papillary endothelial growth. (Case 4.)

Melano-epitheliomata are generally considered to be extremely malignant, giving rise to early and widespread metastasis. Case 1 is typical. The original lesion was very small, and apparently it was completely removed, but in spite of this the fatal outcome was comparatively rapid. The widespread metastasis was exemplified by the metastatic growths demonstrated in roentgenological examination of the thorax. Radium applied locally and over the groin did not cause appreciable retardation of the progress of the disease. In this case, the gross appearance of the original tumor was not unlike that of a comparatively innocent but painful thrombotic external hæmorrhoid. The fact that the intensity of the symptoms increased for 3 weeks instead of subsiding, as is characteristic of the pain in cases of thrombotic external hæmorrhoids, was sufficient to warn the examiner that the condition deserved added consideration, and the "spotty pigmentation" in the skin suggested the possible underlying pathological condition.

Case 2 is more confusing, for the diagnosis was revealed only when the pathologist made his routine examination of the tissue removed at operation. The mass discovered was very small, and the anal canal was scarred from previous treatment. The scar tissue so distorted the canal and the flexibility of the tissue in this region, that the tumor could not be discovered by gross examination or palpation.

Hæmangio-endotheliomata are relatively more rare than melano-epitheliomata, are less rapid in rate of growth, and metastasis is less frequent. There is less information in the literature concerning these growths, but metastasis has been observed. MacCallum cited a case in which the original growth was in the small intestine and there were hundreds of metastatic growths in the liver. In another case the tumor arose in the region of the scapula of a boy. This tumor was partially resected, but it rapidly recurred and there was metastasis to the lungs. MacCallum stated that the tumor suggested a hypernephroma, but that no tumor was found in the kidneys, suprarenal glands, or elsewhere, and that the metastatic growths were about the size of a pea. The same author mentioned Calmers, who cited a case in which metastasis was to the internal organs.

Case 3 closely parallels Case 1. The duration of the growth was similar to that in Case 1 as was its anatomical situation. In Case 3, however, the growth was painless, although increasing in size. Likewise, it resembled a thrombotic external hæmorrhoid, but the total absence of pain pointed to some other type of pathological process. The fact that the patient had previously been informed that she had hæmorrhoids, and the fact that she had an abnormally intense fear of cancer, account for her close observation and prompt effort to seek a remedy for this condition.

To carry on the comparison of cases: Case 4 is very similar to Case 2 in that the neoplasm was discovered at the time of the routine examination of tissue by the pathologist.

These cases evoke consideration of several important phases in the diagnosis of anorectal lesions. It has been stated frequently that actual examination of the anus and rectum is more important than is the history obtained from patients relative to lesions of these parts. However, the history cannot be totally ignored, as is well illustrated by Cases 1 and 3. It is true that examination is of greater relative value than the history when considering anorectal lesions, but the history frequently will point out the salient differences in lesions that appear to be similar, and it cannot be too lightly considered.

Two of the cases described prove the value of the routine microscopic examination of tissue removed at operation. This routine is almost universal when large masses of tissue are removed or when a diagnosis is obscure, but it is less rigidly maintained with regard to the comparatively small amounts of tissue removed during an anorectal operation. This is especially true when hæmorrhoidectomy is performed.

The prognosis in cases of melano-epithelioma is grave, but it is not beyond reason to expect that if the growth could be discovered soon enough, the prognosis could be altered favorably. It is worthy of note that McEuen has used roentgen therapy in six cases of melanosarcoma and has reported two cures. In general, it is the feeling that these tumors are comparatively resistant to radium and roentgen therapy. Generally the outlook is much more optimistic for patients who are afflicted with hæmangio-endotheliomata. These growths occur frequently in parts of the body where they attract attention rather early and surgical excision brings about cure in a large number of cases. The progress of the growth is slower and it is more responsive to the effects of radium and roentgen therapy.

It is interesting, but of little importance, that melano-epitheliomata in this group occurred in men and the hæmangio-endotheliomata in women. A case of melanoma in a woman has just been reported by Marino. Kraker reported a case in which melanosarcoma occurred so low in the rectum that the pathologist discovered epithelial cells of the squamous type on one border of the

tissue removed. Goldblatt also reported a case of melanoma in which the tumor projected from the rectum. The patients whose cases are here reported were within the so called cancer age, but otherwise their ages were of no significance.

The differential diagnosis of anorectal lesions is not emphasized as frequently as is the differential diagnosis of pathological processes occurring in other parts of the body. These cases serve emphatically to point the need of considering the wide range of pathological possibilities in this region and also the close resemblance between the most benign and most malignant lesions.

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RENAL TUBERCULOSIS AND NEPHROLITHIASIS AS ASSOCIATED DISEASES

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THE only available statistics as to the frequency of an association of renal tuberculosis and nephrolithiasis in a large number of cases are those of Brongersma, Wildbolz, Crenshaw of the Mayo Clinic, and Tardo.

Brongersma had never observed the combination in 1000 cases of renal tuberculosis. Wildbolz has seen the association in only 14 (1.4 per cent) of 1000 cases. In a recent paper, "Calcification in Renal Tuberculosis," Crenshaw of the Mayo Clinic states that there was roentgenographic evidence of definite calcification in 131, or 7.1 per cent of 1817 cases. No distinction is made as to how many of the 131 cases represented simply calcification in the form of lime deposits in a tuberculous kidney and as to how many were cases of true, i.e. well formed, calculus formation found in association with renal tuberculosis. Braasch and Olson of the Mayo Clinic, in a paper published in 1919, stated that, in 19 of 1079 cases of renal tuberculosis, a true calculus formation was found. Tardo quoted by Gottstein collected 10 cases of calculus formation in 1047 cases of renal tuberculosis operated on in Italian clinics.

It is very important, as will be seen later under "General Considerations," to make a distinction between simple calcification and true stone formation in tuberculous kidneys from the standpoint of both diagnosis and of prognosis.

I have been able to find reports of 35 cases published since 1920 to which 5 personally observed cases are added. Although the total number of cases of an associated renal tuberculosis and nephrolithiasis or ureterolithiasis is comparatively small, the possible occurrence of such an association should be constantly borne in mind. In fact, Wildbolz goes so far as to say that one should suspect an associated renal tuberculosis in every case of renal or ureteral calculi associated with infection.

PERSONAL CASES

CASE 1. Clinical diagnosis: renal tuberculosis, confirmed by operation. Small calculus in cavity of tuberculous kidney.

Patient was a female aged 29 years, who had had burning on urination and frequency for a year. She had an attack of renal colic 6 months before my first examination, which revealed evidences of right renal tuberculosis. Nephrectomy was performed and the specimen showed two small calculi in one of the cavities (Fig. 1) of a kidney which was the seat of a moderately advanced caseocavernous type of tuberculosis.

The diagnosis of renal tuberculosis was so apparent without roentgenographic evidence, that the latter seemed superfluous. Possibly the passage of a similar calculus had been the cause of the severe renal colic 6 months before. The calculi found at the time of operation were still attached to the wall of the cavity and had evidently been formed around a nucleus of necrotic material.

CASE 2. Clinical diagnosis: calculous pyonephrosis. History of passage of calculi. Multiple shadows over right kidney region. Nephrectomy. Multiple soft, partly-formed phosphatic calculi in cavities of tuberculous pyonephrosis.

A female, aged 38 years, had had frequent attacks of severe pain over the right kidney region, associated with chills and fever. These attacks had been noted over a

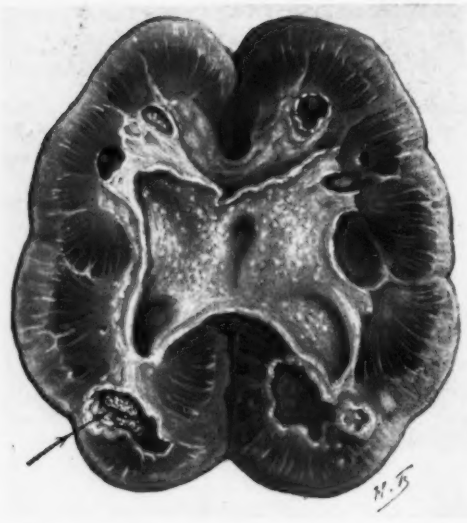

Fig. 1. Tuberculous kidney from Case 1. Note two small calculi lying in a cavity at lower pole. The arrow points toward the calculi. The severe renal colic in this case was probably due to the passage of a similar small calculus.

period of 5 years. The history revealed the passage of calculi. Multiple shadows of varying density (Fig. 2) and a palpable mass were noted over the right kidney region. The diagnosis (from these and other findings) was calculous pyonephrosis. Nephrectomy was done. Examination of the specimen revealed an advanced stage of caseocavernous type of tuberculosis with almost every cavity filled by a soft calcareous material, which in places had assumed the form of a true calculus (Fig. 3).

The irregular contours and variation of density of the shadows (Fig. 2) so characteristic of calcified tuberculous lymph nodes and of calculi formed in tuberculous kidneys should have led us to suspect the latter condition with secondary calculus formation.

CASE 3. Clinical diagnosis: calculous pyonephrosis. Mass and two shadows over right kidney. Marked pyuria. Previous operation for bladder stone. Nephrectomy. Coral calculus in pelvis and a smaller one in cavity of a tuberculous pyonephrosis.

A boy, 8 years old, had had a vesical calculus removed at age of 5 years. Two shadows (one branching and one smaller) were noted over the right kidney region (Fig. 4) and there was also a mass in the same region. Marked pyuria on right side was also noted. Nephrectomy for supposed non-tuberculous calculous pyonephrosis was carried out. Examination of the specimen revealed a well-formed, branching and a smaller, round calculus, lying respectively in the pelvis and one of the cavities of a kidney which was the seat of an advanced tuberculosis (Fig. 5).

The history of an operation for vesical calculus and the presence of shadows which resembled, in every respect, those found in nephrolithiasis, resulted in the erroneous diagnosis of non-tuberculous infection.

CASE 4. Clinical diagnosis: infected stone kidney. Oval shadow and mass over the right kidney region. Operation revealed an oval calculus in the pelvis of the tuberculous kidney.

A female, aged 57 years, had recurrent pain over the right kidney and frequency of urination for past 3 years. Right ureteral rigid and gaping. Unable to catheterize right ureter. Crescentic shadows were present over the right kidney region (Fig. 6). The diagnosis made was renal calculus and non-tuberculous pyelonephritis. Examination of kidney after operation (nephrectomy) revealed a well formed, large calculus filling the pelvis of a kidney which was the seat of an advanced caseocavernous form of tuberculosis (Fig. 7).

The appearance of the ureteral (right) orifice should have led to the suspicion that the concomitant infection was not of an ordinary pyogenic character.

CASE 5. Clinical diagnosis. Renal tuberculosis. Roentgenographic examination not made. At operation large coral calculus in pelvis of a tuberculous kidney.

A male, aged 46 years, gave a history of amputation of the limb for tuberculosis. A marked left pyuria was noted; elimination of indigocarmine, absent. Many ulcers were noted around the left ureteral orifice. Stain was positive for tubercle bacilli in the urine from the left kidney; hence nephrectomy for renal (left) tuberculosis. Examination of specimen revealed a large coral calculus in the renal pelvis of a kidney which was the seat of an advanced caseocavernous type of tuberculosis. Some time later, operation was performed for tuberculosis of the epididymis.

This case shows the necessity of routine roentgenographic examination (plain film at least) in all cases of renal tuberculosis.

In none of these 5 cases was the correct diagnosis of an association of renal calculus and tuberculosis made. In Cases 2, 3, and 4, we believed the concomitant infection to be of a non-tuberculous character. This, as will be shown under "General Considerations," has been true of the majority of the reported cases. In Case 1, the calculus was probably too small to be recognized by roentgenography. In Case 5, such an examination was not considered necessary.

GENERAL CONSIDERATIONS

Types of calcification and calculus formation in tuberculosis of the kidney. In order to make a correct pre-operative diagnosis of the association of calculus formation and renal tuberculosis, it is necessary to distinguish calcification in a tuberculous kidney and true calculus formation as shown in Cases 3, 4, and 5, just cited.

1. *Calcification in a tuberculous kidney.* This question has been very thoroughly studied by Braasch and Olson in 1919 and more recently

Fig. 2. Shadows of soft phosphatic calculi as found before operation in Case 2. Note the irregular contour and variation in density of the shadows.

(1930) by Crenshaw who makes the following division:

Group 1. Multiple scattered small areas, generally due to lime deposits. These are seen (a) as single, elongated, irregular faint streaks or (b) multiple punctate areas, scattered over a large portion of the kidney, usually in one of the poles.

Group 2. Single (Fig. 1) or several isolated areas of calcareous deposit which are easily confused with stone. These shadows are of several varieties:

a. Of irregular outline, with fainter shadow than that of stone and varying in size (as in Case 2, Fig. 2).

Fig. 4. Roentgenogram in Case 3. Note shadow of a branching calculus and of a smaller one. (Compare with Fig. 5.)

Fig. 3. Kidney from Case 2. Note the soft phosphatic calculi which fill and assume form of nearly every cavity and dilated calices.

b. Shadow of very irregular consistence and outline, somewhat resembling filigree work.

c. Definite shadows with a density and contour suggestive of stone.

Group 3. Large, regular rounded shadows of variable density in their various portions. As a rule, the kidney is of putty-like consistence in such areas. The shadow may vary in density in different portions of the kidney, some portions being so dim (Fig. 8) as to be scarcely discernible while in complete caseation the shadows may assume the outline of a complete cast (Fig. 9) of the kidney and are irregularly divided into lobules.

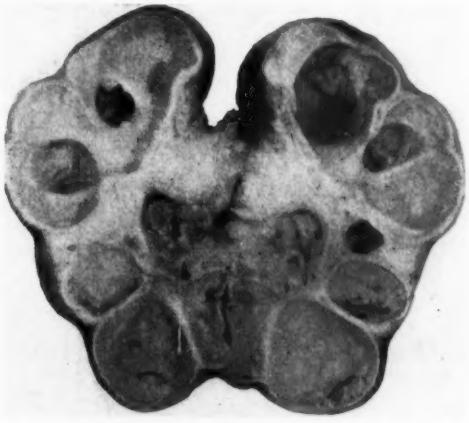

Fig. 5. Kidney from Case 3. Note the typical tuberculous pyonephrosis with a large calculus in the renal pelvis and a smaller one in a cavity.

Fig. 6. Roentgenogram from Case 4 showing irregular or crescentic shadow in right kidney region, due to relatively large calculus (see Fig. 7).

Fig. 7. Kidney from Case 4. Note the relatively large calculus in the pelvis of a kidney which is the seat of advanced tuberculous changes.

2. *True calculus formation in a tuberculous kidney.* There is much difference of opinion in regard to which is primary, the tuberculosis or the calculus. If the latter is composed of oxalates or urates, it seems logical to believe that the calculus formation was independent of the tuberculosis. In the case of calculi composed of calcium carbonate and especially of calcium phosphate, the secondary origin seems most probable. The shadows due to true calculi do not differ in intensity or contour from those observed in non-tuberculous cases. This is well shown in Case 3 (Fig. 4). One can readily exclude the majority of extrarenal conditions such as calcified retroperitoneal lymph nodes by the use of the opaque catheter with or without pyelography. The shadows due to such nodes are, as a rule, characterized by an irregular, moth-eaten contour and a variation in the intensity of the shadow. Occasionally, these criteria cannot be depended on and uretopyelography (retrograde) must be employed (Fig. 10).

Fig. 8. Moderately advanced degree of diffuse calcification in a tuberculous kidney. (Courtesy of Dr. J. L. Crenshaw and of the Mayo Clinic.)

Fig. 9. Very advanced degree of diffuse calcification in a tuberculous kidney. (Courtesy of Dr. J. L. Crenshaw and of the Mayo Clinic.)

Fig. 10. Roentgenogram from case in which the shadows of calcified retroperitoneal lymph nodes resembled those due to renal calculi. Note their change in position and their extra-ureteral location as shown in ureteropyelogram.

Sermet has recently reported a case in which three calcified tuberculous nodes yielded shadows which were interpreted as calculi lying in the pelvis of a tuberculous kidney. At operation, three calcified lymph nodes were found lying in close proximity to the renal pedicle.

One must also bear in mind that a true renal or ureteral (Fig. 11) calculus may be associated with a shadow due to a tuberculous lymph node.

Clinical groups. All of the cases thus far reported may be grouped as follows:

Group 1. Calculus and tuberculosis on the same side (Table I). Of the 40 cases (including my own 5 cases) reported since 1920, the majority, 26 cases, belong in this group. They may be summarized as follows:

Pre-operative diagnosis (26 cases)

	Cases
Renal or ureteral calculi with infection	13
Same and renal tuberculosis	1
Non-tuberculous pyonephrosis	2
Renal tuberculosis only	8
Suspected renal tuberculosis	1
Suspected renal tuberculosis and calculus	1

Thus we see that in only one case (Case 6 of Group 1) was the correct diagnosis made before operation.

Roentgenographic evidence of calculi. Of the 19 cases, in which the results of the roentgenographic examination are given, only 3 yielded negative results. In 1 of my own cases (Fig. 2) the shadows were due to deposits of lime salts rather than to true calculi.

Fig. 11. Simultaneous presence of ureteral calculus in the pelvic portion of the ureter and of a calcified lymph node. (Courtesy of Dr. Joseph S. Eisenstaedt.)

The same was true of one of Howald's cases.

Group 2. Tuberculosis on one, calculus on the opposite side. The 5 cases in this group are of especial importance. At intervals varying from 26 days to 1 year, after a nephrectomy for renal tuberculosis, an anuria due to an obstructing calculus in the ureter of the remaining kidney, developed in the 5 cases of this group. In one of the cases (Grondahl), the roentgenographic examination was negative at the time the nephrectomy was performed. In the 4 others, there is no mention of such an examination.

Why calculus formation occurs in the remaining kidney following nephrectomy for tuberculosis is still being debated. Howald is of the

TABLE I.—SUMMARY OF CASES. GROUP 1. CALCULUS AND TUBERCULOSIS ON SAME SIDE

Author	Clinical diagnosis	X-ray	Treatment	Specimen	Course
1. Barney and Mixter J. Urol., 4, 391, 1920	Infected stone kidney. Retracted right ureteral orifice	Positive (large coral shadow)	Nephrectomy	Tuberculosis and calculus (renal)	
2. Bitschai Ztschr. f. Urol., 17, 463, 1923	Tuberculous pyonephrosis	Not given	Nephrectomy	Same	
3. Phélip J. d'urol. 16, 486, 1923	Ureteral calculus. Bladder and guinea pig negative for tuberculosis	Shadow of calculus in upper third of ureter	Nephrectomy	Tuberculosis and calculus (ureteral)	
4. J. Salleras Semana med., 31, 1106, 1924	Nephrolithiasis	Large and small shadow in right kidney region	Nephrectomy	Tuberculosis and multiple calculi (renal)	
5. K. Mészáros Arch. f. klin. Chir., 143, 415, 1926	Suspected renal tuberculosis. Stain negative. Severe hæmaturia	Not mentioned	Nephrectomy	Tuberculosis and small calculus in pelvis	
6. Adler-Racz Ztschr. f. urol. Chir., 25, 303, 1928	Renal tuberculosis and ureteral calculus (same side)	Positive for ureteral calculus	Nephrectomy	Advanced renal tuberculosis	
7. R. F. O'Neil Tr. Am. Ass., G. U. Surg., 21, 27, 1928	Suspected renal tuberculosis associated with renal calculus	Positive for renal calculus	Nephrectomy	Tuberculosis and renal calculus	
8. B. A. Thomas J. Urol., 22, 433, 1929	Non-tuberculous pyonephrosis	Negative	Nephrectomy	Tuberculosis and large renal calculus	
9. Howald Ztschr. f. urol. Chir., 27, 118, 1929	Renal calculus	Positive (large shadow)	Pyelotomy		Report of guinea pig inoculation from urine taken before operation was reported positive after pyelotomy for renal calculus had been performed
10. Idem	Infected stone kidney	Positive (3 fairly large shadows)	Nephrotomy for calculi	Examination of a nodule excised from kidney at operation revealed tuberculosis	
11. Idem	Renal calculus	Positive (small shadow)	Pyelotomy for calculus		Same as in Case 9, but in this case there was a fistula (postoperative)
12. Idem	Non-tuberculous pyonephrosis	Negative	Nephrectomy	Found tuberculous pyonephrosis and two calculi	
13. Idem	Renal tuberculosis	Negative	Nephrectomy	Found calculus in pelvis	
14. Idem	Same	Same	Nephrectomy	Thick, fragile incrustation in renal pelvis	
15. Sermet J. d'urol., 30, 441, 1930	Renal tuberculosis	Positive (large shadow)	Nephrectomy	Tuberculosis and large coral calculus	
16. Idem	Same	Same	Nephrectomy	Tuberculosis and two hazelnut sized calculi	
17. Olsen J. Urol., 23, 81, 1930	Calculous pyonephrosis	Positive (large and several smaller shadows)	Nephrectomy	Tuberculosis and multiple large calculi	
18. Idem	Renal tuberculosis	Negative	Nephrectomy	Tuberculosis and large calculus blocking outlet of renal pelvis	
19. Taylor Urol. & Cutan. Rev., Jan. 1934	Calculous pyonephrosis	Positive. Two distinct shadows	Nephrectomy	Tuberculosis and a calculus imbedded in one of the cavities	
20. Idem	Renal calculus and hydronephrosis	Positive. Triangular shadow	Nephrectomy	Tuberculosis and multiple calculi (one large and several smaller in pelvis)	

TABLE I.—SUMMARY OF CASES. GROUP 1. CALCULUS AND TUBERCULOSIS ON SAME SIDE—Continued

Author	Clinical diagnosis	X-ray	Treatment	Specimen	Course
21. Taylor Urol. & Cutan. Rev., Jan. 1934	Calculous pyonephrosis	Not mentioned	Nephrectomy	Tuberculosis and renal calculus	
22. Eisendrath (Case 1)	Renal tuberculosis	Not taken	Nephrectomy	Tuberculosis and small calculus in cavity	
23. Idem (Case 2)	Multiple calculi and pyelonephritis	Positive. Multiple shadows	Nephrectomy	Multiple soft calculi in cavities of advanced renal tuberculosis	
24. Idem (Case 3)	Calculous pyonephrosis	Positive. Coral and smaller shadow	Nephrectomy	Advanced stage of renal tuberculosis with coral calculus in renal pelvis and smaller one in a cavity	
25. Idem (Case 4)	Renal calculus and advanced non-tuberculous pyelonephritis	Positive. Crescentic shadow	Nephrectomy	Oval phosphatic calculus lying in pelvis of tuberculous kidney	
26. Idem (Case 5)	Renal tuberculosis	Not taken	Nephrectomy	Large coral calculus in pelvis of a tuberculous kidney	

TABLE II.—GROUP 2. TUBERCULOSIS ON ONE SIDE AND CALCULUS ON OPPOSITE SIDE

Reference	Clinical diagnosis	X-ray	Treatment	Specimen	Course
1. Grondahl Abstr. in Ztschr. f. urol. Chir., 13, 337, 1923	Right renal tuberculosis	Negative for ureteral calculus	Nephrectomy for tuberculosis of right kidney	Tuberculous pyonephrosis	Anuria (4 weeks after right nephrectomy) due to left ureteral calculus which was removed by ureterotomy
2. Ijira and Akita Abstr. in Ztschr. f. urol. Chir. 29, 349, 1930	Renal tuberculosis	Not given	Nephrectomy for renal tuberculosis	Tuberculous pyonephrosis	Anuria 26 days after nephrectomy. Unable to pass ureteral catheter beyond calculus in opposite ureter, hence pyelotomy and relief of anuria by retrograde passage of catheter alongside obstructing ureteral calculus
3. Idem	Renal tuberculosis	Not given	Nephrectomy	Tuberculous pyonephrosis	Anuria (70 days after nephrectomy) due to calculus obstructing opposite ureter. Anuria relieved by passage of ureteral catheter. Stone passed 6 days later
4. Howald Ztschr. f. urol. Chir., 27, 118, 1929	Right renal tuberculosis	Not given	Nephrectomy	Tuberculous pyonephrosis	Anuria (1 year after nephrectomy) due to ureteral calculus on opposite side. Pyelotomy and removal calculus later
5. Idem	Renal tuberculosis	Not given	Nephrectomy	Tuberculous pyonephrosis	Anuria (1 month after nephrectomy) due to calculus in opposite ureter. Removal calculus by ureterotomy. Relief of anuria

opinion that such calculus formation is favored by the forced feeding in sanatoria.

Group 3. Bilateral renal or ureteral calculi and unilateral tuberculosis (*Table III*). There were only 4 cases in this group. In Fowler's case, a nephrectomy was performed for the associated lesions. In Irisawa's case, a large coral calculus was removed from one kidney and a nephrectomy for the associated lesions performed on the other side. In one of Howald's cases, nothing had been done, and in the other case, a nephrectomy.

Group 4. Bilateral renal tuberculosis and unilateral stone formation. Only 5 cases belong in this group. Of interest are the cases of D'Agata and of Kuzmeckij. In the former, a large calculus was removed by nephrotomy from a tuberculous kidney. In Kuzmeckij's case a calculous anuria developed 1 year after nephrectomy for renal tuberculosis. Autopsy revealed the presence of two calculi obstructing the ureter of the remaining tuberculous kidney.

Group 5. Bilateral renal tuberculosis and lithiasis. Gottstein cites 4 cases (those of Helmut, Joseph, Kuemmell and Liebermeister). They are of little practical clinical interest except from the standpoint of diagnosis.

TREATMENT OF THE VARIOUS GROUPS

Group 1. Tuberculosis and calculus on same side. It is generally accepted that nephrectomy

TABLE III.—GROUP 3. BILATERAL CALCULI AND UNILATERAL TUBERCULOSIS

Author	Clinical diagnosis	X-ray	Treatment	Specimen	Course
1. H. A. Fowler J. Urol., 5, 345, 1921	Bilateral renal calculi	Positive. Shadow (navy bean size) in pelvis of left kidney and much larger in right renal pelvis	Nephrectomy (left)	Tuberculosis (advanced stage) with calculus size of large bean in pelvis	
2. Irisawa Abstr. in Ztschr., f. urol. Chir., 25, 257, 1928	Bilateral renal calculi	Positive for calculi in both kidneys	Nephrotomy (right) for large coral calculus. Nephrectomy (left)	Left tuberculous kidney had small calculus in a cavity	Found acid-fast bacilli in the calculi
3. Howald Ztschr. f. urol. Chir., 27, 118, 1929	Bilateral calculi (renal and ureteral) and unilateral renal tuberculosis (left)	Positive	Nothing done up to time of publication of article		
4. Idem	Bilateral renal calculi and right renal tuberculosis	Positive. Small shadow in left kidney region and two distinct shadows in right kidney region	Right nephrectomy	Calcified caseated areas	

TABLE IV.—GROUP 4. BILATERAL RENAL TUBERCULOSIS AND UNILATERAL NEPHROLITHIASIS

Reference	Clinical diagnosis	X-ray	Treatment	Specimen	Course
1. D'Agata Abstr. in Ztschr. f. urol. Chir., 9, 223, 1922	Bilateral renal tuberculosis and unilateral (right) nephrolithiasis	Positive	Nephrotomy for large calculus in right tuberculous kidney		
2. Kuzmeckij Abstr. in Ztschr. f. urol. Chir., 29, 348, 1930	Bilateral renal tuberculosis and unilateral (right) nephrolithiasis	No mention	Nephrectomy (left)	Renal tuberculosis (left)	One year after left nephrectomy, calculous anuria on opposite side. Nephrotomy. Death. Autopsy revealed two phosphatic calculi obstructing right ureter. Kidney (right) showed tuberculous focus
3. Howald Loc. cit.	Bilateral renal tuberculosis and unilateral (right) nephrolithiasis	Positive. Large shadow over right kidney region			
4. Idem	Bilateral renal tuberculosis and unilateral (right) nephrolithiasis	No mention	Drainage of perinephritic abscess (right) from which a calculus was evacuated		
5. Olsen J. Urol., 23, 81, 1930	Bilateral renal tubercu losis and nephrolithiasis	Positive multiple shadows	Nephrotomy for 4 calculi in upper pole of a tuberculous kidney	Only excised segment examined but showed tuberculosis and calculi	One kidney had been removed elsewhere for tuberculosis. Remaining kidney showed calculi and tuberculosis

is the best method of treatment, at the present time, for a case of unilateral tuberculosis unless some contra-indication, outside of the urinary tract, exists. The same indication exists when either calcification or true calculus formation is an associated condition.

If one has overlooked the existence of a renal tuberculosis in a case of unilateral renal or ureteral calculus, the following dangers may be present: (a) the persistence of a postoperative fistula; (b) the chances of recurrence of calculi are greatly increased.

Every case of renal or ureteral calculus associated with infection, should be examined for the possible co-existence of a renal tuberculosis. In the latter disease, plain roentgenography, at least, should precede nephrectomy, in order to be able to detect the presence of true calculus formation as an associated lesion. In such individuals, the probability of calculus formation in the remaining kidney, at some future date, is probably greater than when renal tuberculosis exists alone.

Group 2. Tuberculosis on one side and calculus on the opposite side. If both conditions have been recognized at the first examination of the patient, Howald advises removal of the tuberculous kidney first and of the calculus at a later sitting. The writer believes the danger of a postoperative anuria is greatly lessened in the case of a ureteral calculus on the opposite side, by making every effort first to deliver the calculus by non-operative or operative means before the nephrectomy. The treatment of the calculous anuria which occurs

after operation, is the same as for that which occurs independently of a previous operation.

Group 3. Bilateral calculi and unilateral tuberculosis. In such cases, Howald advises removal of the kidney which is the seat of the tuberculosis and calculus as a first step. In such cases, the writer would prefer to be guided by the same principles as in ordinary cases of bilateral renal (or ureteral) calculi, viz. to remove the calculi from the better side first.

SUMMARY

1. The association of renal tuberculosis and of true calculus formation occurs in approximately 1.8 per cent of all cases of renal tuberculosis.

2. One must distinguish between calcification which is found in about 7 per cent of all cases of renal tuberculosis and true calculus formation.

3. Forty cases, reported since 1920, the majority of which are instances of true calculus formation in tuberculous kidneys (on the same or opposite side), are tabulated; 5 of the 40 cases are personal observations of the author.

4. The cases can be placed in four clinical groups. The first and second of these are of especial importance. In the former, if one overlooks the concomitant tuberculosis in a case of renal or ureteral calculus, there is the danger of a persistent postoperative fistula as well as of early recurrence of calculi.

The only case in this first group (26 cases) in which a correct pre-operative diagnosis (of associated calculus and tuberculosis) was made is that of Adler-Racz (Table I).

In the second group, 5 cases, reported since 1920, of calculous anuria following nephrectomy for tuberculosis, at intervals of 26 days to 1 year, are cited. A number of similar cases were published prior to 1920 by Eliot, Kuemmell and others.

Plain roentgenography even in cases of well marked renal tuberculosis should be considered a routine measure in order to detect the presence of renal or ureteral calculi.

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THE TREATMENT OF ACUTE SUPPURATIVE ARTHRITIS

Report of Thirty-Six Cases Treated by Operation

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THE following study of the end-results in the surgical treatment of acute suppurative arthritis is based upon 36 cases of this disease in which operations were performed at the New York Orthopædic Hospital during the 15 years from 1918 to January 1, 1933. It will include only the cases in which movable joints were affected, thus excluding those in which the infection involved the sacroiliac joints, where restoration of motion is not desired in the treatment. Also, because gonorrhœal arthritis is a separate and distinct disease clinically and pathologically, rarely proceeding to suppuration, seldom if ever requiring incision, no cases of this disease are included in the present study. Thus the report will deal only with acute non-specific purulent arthritis in movable joints.

HISTORICAL

The attitude of the medical profession toward this disease has been a singularly variable one. There has always been respect for it; but the forms of treatment advocated for its cure have been many, and these have often been diametrically opposed to each other in theory. Whether to incise or to aspirate, to mobilize or to immobilize, to disinfect or to irrigate, whether or not a drain should be inserted—these are questions about which there have been many differences of opinion.

In general it may be said that the chief concern of seventeenth and eighteenth century surgeons in such cases was to preserve the life of the patient; that the nineteenth century surgeon tried, in addition, to save the affected limb; and that with the beginning of the twentieth century came the idea of preserving the *function* of suppurative joints.

The attitude of the sixteenth century surgeons toward this disease is well expressed by Peter Lowe, who, in his *Discourse on the Whole Art of Chyrurgerie* (1597), writes of "The tumor or paine in the knees" as follows:

> If it tend to suppuration, beware to open it, for it is forbidden by our ancients to make deepe incisions under the rotule of the knee, because those parts are both sensible and painefull, and oftentimes evill accidents ensue; so you shall use corroborative remedies, and anodynes, evacuating the matter and siccatrizing the wound, as you have heard in others.

The seventeenth century surgeon, Richard Wiseman, was the first to differentiate between acute suppuration in joints and a condition which he called "tumor albus," and which, after Koch's time, was recognized as tuberculosis. The failure to distinguish between these two diseases, however, is apparent in the works of writers much later than Wiseman, and possibly accounts for much of the variation in the methods of treatment of purulent arthritis. Even today this differential diagnosis is not a simple one.

During the seventeenth and eighteenth centuries there was a passion for amputation of limbs, often with small provocation, and pyarthrosis was not the least of the indications for removal of a limb. Joint suppuration was considered a serious threat to the patient's life, and preservation of the limb was not considered feasible. Early in the nineteenth century a revolt against amputations was led by Sir William Fergusson, Astley Cooper, Brodie, and others, and it became the mode to try to save the limb as well as the life of the patient. The conception of the treatment of joint infections at this time is summarized by Sir Benjamin Brodie:

> However formidable such cases of rapid suppuration and joint destruction may be, they are now much under the control of art, so that the patient will in many instances recover, preserving the limb, but not the motion of the joint, which remains immovable. . . . If the joint be purulent, a free opening should be made in a depending situation. It is important that the operation be not long delayed, and that the opening should be sufficiently large to allow the matter to flow out spontaneously; but all this will be of little avail, unless the joint be kept in a state of most complete immobility.

The twentieth century ushers in a variety of new ideas in the treatment of this old disease. It suddenly becomes "criminal," according to one author (Cotton), or "an outrage" according to another (Reich), to treat an infected joint by the "ancient method" of drainage and the introduction of wicks; the one writer is sure that the proper

treatment is to close the joint tightly after incision and washing out of the pus, the other is just as sure that aspiration and lavage is the only treatment. Other authors in this period advocated "disinfection" of the joint, and many were the kinds of chemicals recommended for this purpose. Chemical disinfection reached its zenith during the early years of the World War, in the form of the Carrel-Dakin irrigations.

The idea of preserving motion at the infected joint is relatively recent, and it is not yet by any means universally accepted. Even today there are surgeons whose attitude toward such joints is: "Let them ankylose in good position." To whom the credit should go for first introducing the principle of maintaining function in purulent joints is not known, but it was preached at the beginning of this century by Professor Erwin Payr, of Leipzig.

In 1881 Macnamara described the use of drainage tubes in the incisions into purulent joints; drains, however, were undoubtedly used long before this. Over no other question in the treatment of suppurative arthritis has there been so much controversy. Up to 1914 their use seems to have been general, but since then there has been widespread objection to the insertion of any foreign body into an infected joint. It is argued that drains will cause additional necrosis of tissues, especially of cartilage, by pressure; or that they may cause thick walled sinuses, or the partitioning of the joint by firm adhesions. By the more vehement writers their use has been denounced as criminal; by others, as unnecessary. Dr. Russell A. Hibbs, late chief surgeon of this hospital, always maintained that it was the *pus* which destroyed the tissues in such a joint; that the obvious treatment was to evacuate this by the most effective possible means; and that a properly used drain, instead of damaging the joint, was the simplest and most efficient means of obtaining such a result.

During the World War, Willems, a Belgian army surgeon, introduced a method for treating suppurating joints following penetrating wounds, which was hailed by many as revolutionary, and as "the most valuable acquisition which the surgery of the war has given us" (Cohn). The principles of this method were: (a) wide arthrotomy, followed by (b) immediate, prolonged, full active motion, and (c) walking on the affected limb as soon as the patient's temperature fell below 100 degrees F. Some observers reported that pus was actually squirted out of the wounds at each step when Willems' patients walked. The treatment was calculated to cause thorough drainage of the pus by the active motion and weight-bearing, and it apparently was successful in some cases. The stoicism required of a patient in undergoing this method of treatment is, however, not common in peace-time civil populations, as is shown in the case reports which have appeared in the literature. Willems himself, in his original report, listed three ankyloses and one secondary resection in eleven purulent knees treated by his method, 36 per cent failures. This is somewhat better than the results obtained by other surgeons who have made case reports. For example, Depage and Delray had 42 per cent failures in 31 cases; Everidge had 60 per cent failures in 20 cases; Duval had 40 per cent failures in 5 cases; Cotte had 100 per cent failures in 8 cases; Cotton had 100 per cent failures in 2 cases.

Fig. 1. Suppurative arthritis of right hip, before operation. Marked effusion, no bone destruction. Duration of symptoms, 8 days. (Case 1, Table I.)

Launay, however, had 2 "successes" in 2 cases. No other case reports have been found in the literature. Desgouttes and Duguet, two contemporary French surgeons, report no cases of their own, but agree that the Willems treatment, unnecessary in mild cases, is impossible and contra-indicated in severe ones. The last named author advises resection for a purulent joint, and sums up the modern French attitude by saying: "In these grave arthritides cure is only obtained by ankylosis, and it is exactly this which one obtains by resection. The functional point of view should not be considered." For "mild" cases he recommends arthrotomy and drainage, followed by *immobilization* and vaccine therapy.

Fig. 2. Same case as in Figure 1, 5 days after operation. Note rubber tube drain extending to capsule. The rubber dam drain which extends into the joint can be seen in the X-ray negative, but does not show up in the print.

Fig. 3. Same case as in Figures 1 and 2, 4 years after operation. Except for slight coxa magna and the small calcium deposit in the soft tissues, it is now a normal hip. No limitation of motion, no symptoms, a 4–4–4 result.

Fig. 4. Suppurative arthritis of right hip, complicated by osteomyelitis of femoral neck and head, duration of symptoms 49 days before coming to hospital. (Case 31, Table I.)

Fig. 5. Same case as in Figure 4, 2½ years after ar throtomy and drainage, showing mediocre result whicl is due to previous bone destruction. A 3–4–2 result wa obtained.

The Willems treatment has met varied reception in this country. In some medical schools it is taught exclusively. However, Caldwell, among others, has decried its use, and in 1925 Blake laid down much more conservative principles for the treatment of pyogenic joints. The latter author likened suppurative arthritis to suppurative peritonitis and suppurative pleurisy, and stated: "In both instances, if opened and drained in the early stages, the outcome is often bad; but if treated by the closed method (i.e., repeated aspiration) the results are far better. Aspiration should be repeated until resolution occurs or one becomes convinced that the destruction of tissue, such as cartilage, has taken place, when incision and drainage become necessary." Blake states that this method is particularly applicable to streptococcus infections, and rarely, if ever, to those in which the staphylococcus is involved. He makes no case reports. At the present time most surgeons would probably agree that, whatever may be the possibilities of aspiration in streptococcus infection, a joint with pus in it should have an early diagnosis and early arthrotomy. Destruction of cartilage should thus be obviated rather than waited for.

Chemical disinfection following arthrotomy still has its adherents, and mercuric chloride (Cotton), ether (Duguet), Dakin's solution (Cotton), and Chlumsky's solution (Kortzeborn) have been advocated for this purpose within fairly recent times. Several French authors (Lapointe and Bazy, Miraillié, Thiéry, Wiart) have reported "cures" of suppurating joints by the injection of bacteriophage without arthrotomy. One of these claims the singular good fortune of "curing" a streptococcus suppurative arthritis by injecting a *staphylococcus* bacteriophage into the joint. Such results have not been substantiated by others.

Most of the literature on acute suppurative arthritis is worthless because of the prevalence of opinions based upon theory, and the surprising meagerness of accurate, detailed case reports. Even when cases are reported, the so called "successes" or "cures" or "perfect results" are often meaningless because these terms are not defined by the author; a knee joint with 10 degrees of motion left in it may be a "success" to one surgeon, but by another it would be considered a poor result. The important question of the bacteriology of the cases is rarely discussed, unless it is to say that some were due to the gonococcus, which fact alone should be enough to eliminate such cases from a study of suppurative arthritis.

A series of cases reported by Kortzeborn and Hesse, in 1931, from the Leipzig clinic, constitutes the largest and most completely worked up series found in the literature. These authors prefer to treat a purulent joint by aspiration, injection of Chlumsky's solution, and early motion, although their results in 19 joints so treated were: good function in 4, or 21 per cent; fair function in 4; ankylosis in 5, or 26 per cent; and death in 5 (26 per cent). Cause of death was sepsis in 2 cases, pyæmia in 1, marasmus in 2.

Fourteen of their cases were comparable to those we are about to report; i.e., cases uncomplicated by penetrating wounds or bone injury, treated by arthrotomy and drainage. Their results were unbelievably bad, there being, in 14 cases, 1 death, 1 amputation, 8 bony and 2 fibrous ankyloses; only 2 cases retained partial function. These authors are thus forced to the dismal conclusion that "in all joint suppurations which necessitate a wide opening, one must give up all thought of preserving function." They refrain from using the Willems method because of its inhumanity and the impossibility of carrying it out. The knee was the joint most frequently involved, the staphylococcus the most frequent causative organism. This bacterium was responsible for 7 of their 11 deaths, but the greater percentage of ankyloses occurred with the streptococcus: 45 per cent of the streptococcus cases showed ankylosis, whereas only 25 per cent of the staphylococcus cases in which death did not occur showed this result.

PROBLEMS OF TREATMENT

After a study of the literature on the subject one therefore is left in a dilemma regarding four major problems in the treatment of acute suppurative arthritis:

1. Should a purulent joint be promptly incised, or should it be repeatedly aspirated until cured?

2. Should a joint which has been incised have a drain inserted, to ensure the maintenance of an issue for the exudate?

3. Does complete rest and immobilization offer a better chance for restoration of function than immediate, forced, and prolonged active motion?

4. Does lavage with chemical or biological products offer any hope in the treatment of a purulent joint, with or without incision?

It is hoped that the results obtained in the following series of cases will help to answer these problems.

REPORT OF CASES

In the past fifteen years operations have been performed in this hospital in 36 cases of acute suppurative arthritis.

TABLE I
Group One

Name Sex Age	Joint affected — Duration of symptoms pre-operation in days	Foci of infection? Trauma? Temperature White blood cells	Operation, type of drainage	Culture	Motion begun	Drain removed — Length of follow-up	End-Results		
							Anatomical	Symptomatic	Functional
1. R.B. M 2 yrs.	Hip, R. — 9	Hypertrophy of tonsils T. 102 W.B.C. 34,000, 84%	Posterior drainage. Rubber tube drains sutured in. Traction. 150 c.cm. thick, creamy pus	Hæmolytic streptococcus	Passive on 1st; active on 7th	14th day — 4 yrs.	Affected leg ¾ in. longer than other. X-ray shows slight overgrowth of femoral head and neck, slight calcification in soft tissues outside joint 3	No pain, stiffness, fatigue. Plays all games. Bad weather causes no symptoms 4	Walks with no limp, extension 180, flexion 30, abduction 45, adduction 35, internal rotation 30, external rotation 60 4
2. G.C. F 3 yrs.	Hip, L. — 2	Tonsils. T. 103 W.B.C. 9,500, 54%	Posterior drainage. Rubber tube and rubber dam drains sewed into joint. Traction. 70 c.cm. seropurulent fluid	Staphylococcus aureus	Passive on 1st, active later	40th day — 7½ yrs.	Normal hip to examination and by X-ray 4	No pain, stiffness, ache, or fatigue at any time 4	Motion in left hip same as on right. No limp 4
3. A.D. M 6 mo.	Hip, L. — 14	Tonsils. T. 100 W.B.C. 12,400, 47%	Posterior to greater trochanter. Rubber dam drain into joint. Traction. 6 oz. pus	Non-hæmolytic streptococcus	?	? — 14 yrs.	Shortening of 1 inch. X-ray shows short femoral neck and moderate subluxation 2	No pain, ache, stiffness. Plays all games without handicap 4	Walks with slight limp due to shortening. Extension 180, flexion 30, abduction 45, adduction 40, external rotation 70, internal rotation 10. No telescoping. Trendelenburg's sign negative 4
4. A.G. M 2 yrs.	Hip, L. — 25	Enlarged tonsils. T. 101 W.B.C. 16,800, 34%	Posterior drainage. Tube into joint. Traction. 1 oz. thin pus	Pneumococcus	Passive on 2nd, active ?	6th day — 1 yr.	Normal hip clinically and by X-ray 4	No symptoms. Played all games without handicap. Died 1 yr. 2 mos. after operation of bronchopneumonia at another hospital 4	Had very slight limp. No spasm. Motion normal in all directions, as in right hip 4
5. J.G. M 9 mos.	Hip, L. — ?	Otitis media, purulent cervical adenitis. T. 104 W.B.C. 52,800, 88%	Posterior incision. Rubber tube into joint. Traction. Thick pus under pressure	Hæmolytic streptococcus	?	? — 6½ yrs.	Hip became dislocated, attempts at reduction unsuccessful. Shelf stabilization advised later, but parents refused ?	Unclassifiable. No note ever made as to his symptoms. Not seen by authors ?	Motion exaggerated in all directions. Distinct telescoping ?
6. A.W.K. M 32 yrs.	Hip, R. — 3	Osteomyelitis of left tibia. T. 102 W.B.C. 29,400, 90%	Anterior drainage. Rubber dam drain into joint. Traction. Thin pus	Staphylococcus aureus, non-hæmolyticus	?	21st day — 1½ yrs.	Unclassifiable because of insufficient data		
7. A.L. M 14 yrs.	Hip, R. — 21	T. 104 W.B.C. 16,800. 70%	Aspiration, then anterior incision. Rubber drain into joint. Traction. 100 c.cm. pus	Staphylococcus aureus	?	? — 1 yr.	Unclassifiable because of insufficient data		

TABLE I—Continued

TABLE I—Continued

Group One—Continued

Name Sex Age	Joint affected — Duration of symptoms pre-operation in days	Foci of infection? Trauma? Temperature White blood cells	Operation, type of drainage	Culture	Motion begun	Drain removed — Length of follow-up	End-Results		
							Anatomical	Symptomatic	Functional
8. J.M. F 14 yrs.	Hip, L. — 7	Osteomyelitis of right femur T. 101 W.B.C. 10,700, 72%	Aspiration, then posterior incision. Rubber tube sewed into joint. 25 c.cm. thick pus	Staphylococcus	Passive and active before 6th day	12th day — 5 yrs.	Normal hip clinically and by X-ray 4	No pain, ache, stiffness, even in bad weather. Walks 10 miles without pain or fatigue 4	Extension 180, flexion 40, abduction 50, adduction 25, external rotation 30, internal rotation 45. Walks with slight limp due to shortening in opposite femur 4
9. L.S.J. M 11 yrs.	Hip, R. — 2	Osteomyelitis of r. humerus T. 103 W.B.C. 22,000, 81%	Posterior incision Rubber drain into joint. 1 oz. thin gray fluid	Staphylococcus aureus	Passive immediately, active on 4th	13th day — 5 yrs.	Normal hip clinically and by X-ray 4	No symptoms of any kind at any time. Is on his school track team 4	Extension 180, flexion 30, abduction 50, adduction 45, external rotation 60, internal rotation 45, no limp 4
10. P.T. M 4 yrs.	Hip, R. — 20	Lobar pneumonia 6 weeks before T. 99.4 W.B.C. 14,000, 68%	Posterior drainage. Rubber tube into joint. 8 oz. of thick yellow pus. Traction	Pneumococcus	?	21st day — 1 yr.	Normal hip clinically and by X-ray 4	No symptoms at any time. Had empyema after operation, recovered 4	No limp. Motion normal in all directions 4
11. J.C. M 10 mos.	Knee, L. — 14	Infected operative wound, tumor removed from prepatellar region at another hospital T. 103 W.B.C. 20,000, 71%	Incisions on each side of patella. Rubber dam drain sewed into each. Traction. Small amount of thick pus	Bacillus pyocyaneus	?	? — 2½ yrs.	Normal knee except for slight roughness of femoral condyle by X-ray 4	Very active. No symptoms at any time 4	No limp. Extension 180, flexion 30. No relaxation 4
12. W.G. M 10 yrs.	Knee, R. — 3	Hæmolytic streptococcus septicæmia following mastoidectomy T. 102 W.B.C. 12,950, 65%	Incisions on each side of patella. 2 through-and-through rubber dam drains. Joint distended with pus	Hæmolytic streptococcus	Moved under anæsthesia at 6 weeks	? — 6 yrs.	Has 5 degree flexion deformity; otherwise no deformity 3	Very active. No symptoms 4	Extension 175, flexion 100. Slight limp 2
13. A.G. M 2 yrs.	Knee, R. — 28	Purulent cervical adenitis T. 100.4 W.B.C. 9,000, 62%	Incisions on each side of patella. Rubber tube drain into each. 2 oz. thin pus	Hæmolytic streptococcus	?	? — 9 yrs.	Knee appears normal by X-ray, but has 10 degree flexion deformity 3	Occasionally complains of slight pain, but walks well and is very active 3	Extension 170, flexion 30. Slight limp 3
14. A.S. M 6 yrs.	Knee, R. — 14	Struck on knee by sled three weeks ago. Tonsillitis 3 days ago T. 105 W.B.C. 16,800, 88%	Incisions on each side of patella. Rubber dam drains sewed in. Traction. Thin yellow pus	Non-hæmolytic streptococcus	Moved under anæsthesia on 12th day	? — 3 yrs.	X-ray shows overdeveloped epiphyses and joint space slightly thinned, ¼ in. lengthening of affected leg. Flexion deformity of 15 degrees 3	Denies all symptoms. Bad weather and exercise have no effect 4	No limp or spasm. Extension 165, flexion 35 3

TABLE I—Continued

Group One—Continued

Name Sex Age	Joint affected — Duration of symptoms pre-operation in days	Foci of infection? Trauma? Temperature White blood cells	Operation, type of drainage	Culture	Motion begun	Drain removed — Length of follow-up	End-Results		
							Anatomical	Symptomatic	Functional
15. D.V. M 3 yrs.	Knee, L. — 3	Fall? T. 101 W.B.C. 12,000, 76%	Aspiration followed by incisions on each side of patella. Vaseline gauze drain. Sero-purulent fluid	Staphylococcus and streptococcus	Passive on 1st day	9th day — 4½ yrs.	X-ray shows slight overgrowth of epiphyses, otherwise normal. Normal knee clinically. ¼ inch lengthening of affected leg 4	No pain, fatigue, or ache, even in bad weather or after athletics 4	No limp or spasm. Motion same as in other knee; extension 180, flexion 20 4
16. C.B. F 5 yrs.	Ankle, L. — 6	Fall? Tonsils? T. 101 W.B.C. 16,000, 81%	Medial and lateral incisions. Thick pus. Through-and-through rubber dam drain	Staphylococcus aureus	Passive on 1st, active on 4th	6th day — 4 yrs.	½ inch shortening. Slight enlargement of medial malleolus 3	No symptoms except occasional stiffness on damp days. Plays games all day without fatigue or pain 4	No limp. Motion 105–120 degrees. On right it is 100–135 degrees 3
17. A.F. M 1 yr.	Ankle, R. — 9	Fall, 3 days ago. Tonsillitis. T. 102.6 W.B.C. 30,000, 80%	Lateral incision. Thin watery pus. Rubber dam drain	Non-hæmolytic streptococcus	?	10th day — 1½ yrs.	Ankle normal clinically and by X-ray 4	No symptoms even in bad weather. Plays and runs without pain or stiffness 4	Extension 135, flexion 90. No relaxation 4
18. E.G. F 4 yrs.	Elbow, R. — 2	Osteomyelitis of right femur. T. 103 W.B.C. 42,000, 85%	Aspiration followed by posterolateral incision. Rubber dam drain. 2 oz. thin watery pus	Staphylococcus and streptococcus	?	1st day? — 5½ yrs.	Normal clinically. X-ray normal except for slight enlargement of lower end of humerus 4	No symptoms even in bad weather. Plays all games without handicap 4	Extension 180, flexion 10. Normal pronation and supination. Carrying angle normal 4
19. R.N. M 5 yrs.	Elbow, R. — 5	Pyelitis. Enlarged tonsils. T. 101 W.B.C. 11,200, 73%	Aspiration, repeated 3 days later. Five c.cm. seropurulent fluid each time. T. and W.B.C. became normal in two days	Staphylococcus aureus	Passive on 1st day, active?	— 5 yrs.	Normal elbow. X-ray shows very slight soft tissue thickening 4	No symptoms at any time 4	Normal motion just as in opposite elbow 4
20. V.O. M 1 yr.	Elbow, L. — 1	Fall? Tonsils? T. 102 W.B.C. 12,000, 70%	Aspiration, then posterolateral incision. Rubber dam drain. 15 c.cm. thin green pus	Staphylococcus and streptococcus	Active on 5th day	3rd day — 5 yrs.	Normal clinically and by X-ray. No shortening 4	No symptoms even in bad weather. Full use of arm 4	Extension 180, flexion 30. Supination and pronation normal, carrying angle normal 4
21. D.S. M 12 yrs.	Shoulder, L. — 2?	Osteomyelitis of left femur. T. 101 W.B.C. ?	Posterior incision. 2 oz. seropurulent fluid. Alcohol gauze pack!	Staphylococcus aureus	Active on 1st day	2nd day? — 2½ yrs.	Had numerous recurrences in shoulder, requiring incision, and in leg. Finally taken to another hospital, shoulder and leg still draining 3	o	o
22. J.R. F 7 wks.	Knee, R. — 1	No known focus. T. 100 W.B.C. 15,000, 63%	Aspiration, twice. T. and W.B.C. came down promptly. 5 c.cm. bloody fluid each time	Pneumococcus	?	— 2½ mos.	Normal knee clinically and by X-ray 4	No symptoms. Child still nursing when last seen 4	"Normal range of motion." Not seen by authors 4

TABLE I—Continued

TABLE I—Continued

Group Two

Name Sex Age	Joint affected — Duration of symptoms pre-operation in days	Foci of infection? Trauma? Temperature White blood cells	Operation, type of drainage	Culture	Motion begun	Drain removed — Length of follow-up	End-Results		
							Anatomical	Symptomatic	Functional
23. H.R. F 9 mos.	Knee, L. — 90	No known foci. T. ? W.B.C. 15,200, 51%	One incision medial to patella. Rubber drain into joint. 1 oz. thin pus	No growth	?	3rd day — 11 yrs.	¾ inch shortening. Joint ankylosed. Flexion deformity of 20 degrees 0	No pain at any time. Plays all games 4	Bony ankylosis 0
24. C.M. M 12 yrs.	Knee, L. — 30	Popliteal abscess. T. 105 W.B.C. 25,000, ?%	2 small incisions with rubber drain. Four days later incisions enlarged and Dakin tubes inserted. Much thick pus	No growth	Active before 14th day	Daily irrigations 23rd day — 8 yrs.	Small arthritic lip on tibial condyle. ¼ inch shortening 4	No pain at any time 4	Motion 180–80 degrees, stopped by scar from old compound fracture. No limp 4
25. H.E. M 3 yrs.	Hip, L. — 10	Tonsils removed 3 weeks ago. T. 101 W.B.C. ?	Aspiration, then posterior incision. Drainage tube into joint. 2 oz. thin pus	None taken	?	10th day — 5 yrs.	Normal clinically. X-ray shows normal joint except for slight elongation of neck 4	No symptoms at any time. Very active child 4	Normal motion in all directions, same as in opposite hip. No limp 4
26. O.L. F 1 yr.	Hip, R. — 14	Tonsils. Cough with thick sputum. T. 104 W.B.C. 49,000, ?%	Posterior incision. 5 oz. thick pus. Gauze drain!	No growth in 72 hours	?	? — 7 yrs.	Had osteomyelitis of femoral head, with destruction. Subluxated, telescopes. 1¾ inch short 1	Braces for 3 years. Had empyema later ?	"Free motion in all directions." But unstable. Shelf operation advised, but refused. Disappeared 1

Group Three

Name Sex Age	Joint affected — Duration of symptoms pre-operation in days	Foci of infection? Trauma? Temperature White blood cells	Bone involved; pre- or post-arthrotomy?	Operation (Arthrotomy) Type of drainage	Subsequent operations	Culture — Length of follow-up	End-Results		
							Anatomical	Symptomatic	Functional
27. C.B. F 3 yrs.	Hip, R. — 40	Measles? T. 101.2 W.B.C. 28,600, 66%	Femur and acetabulum at time of arthrotomy	Anterior incision. 1000 c.cm. white, creamy pus. Abscess burrowed subcutaneously. Gauze drains, not into joint (?) Traction	6 subsequent incisions with drainage for osteomyelitis of femur. Hip became ankylosed	Hæmolytic streptococcus — 15 yrs.	Hip ankylosed. 1¾ inches shortening 0	No symptoms. Last operation 5 years ago. General health excellent 4	Ankylosis. Walks with almost no limp 0
28. M.B. F 4 yrs.	Hip, L. — 30	Septicæmia after tonsillectomy	Femur and acetabulum. Femur dislocated on admission	Posterior incision. Femoral head was dislocated by the disease. Reduced, rubber tube drain. Bone not incised. Traction	None	"Staphylococcus" — 2 yrs.	Flexion deformity of 20 degrees. Slight subluxation. X-ray shows coxa plana 2	No pain or spasm. General health good, though ear still drains 3	Flexion to 110, extension 160, abduction 35, adduction 10, "rotation 35." Moderate left limp. Hip stable 2
29. R.D. F 8 mo.	Hip, R. — ?	Tonsils enlarged. T. 101 W.B.C. 17,400, 69%	Femur. Femoral head dislocated and badly eroded preoperation	Posterior incision. Rubber tube drains. Grayish yellow pus	None	Non-hæmolytic streptococcus — 2½ yrs.	Hip still dislocated when last seen 0	No pain, no drainage. Walks with a hip splint 2	Hip still dislocated. Stabilization operation advised 0

TABLE I—Continued

Group Three—Continued

Name Sex Age	Joint affected / Duration of symptoms pre-operation in days	Foci of infection? Trauma? Temperature White blood cells	Bone involved; pre- or post-arthrotomy?	Operation (Arthrotomy) Type of drainage	Subsequent operations	Culture / Length of follow-up	End-Results: Anatomical	Symptomatic	Functional
30. K.G. F 8 yrs.	Hip, L. / 21	T. 100 W.B.C. 16,000, 80%	Femoral neck. Pre-operation	Posterior incision. Tube and rubber dam. Bone not touched. 15 c.cm. purulent fluid	Sequestrectomy of upper ⅓ of femur 1½ yrs. later. Did not connect with hip	"Staphylococcus and streptococcus." / 6 yrs.	½ inch short. X-ray shows no evidence of disease. Normal contour. Epiphysis shows union 3	No pain, stiffness. Plays all games without fatigue or handicap 4	Flexion 60, extension 180, abduction 20, adduction 20, external rotation 30, internal rotation 30. No limp 3
31. D.H. M 8 yrs.	Hip, R. / 49	Struck on hip 1 week ago. T. ? W.B.C. 10,000, 49%	Femoral neck. Pre-operation	Anterior incision. Large amount thin turbid fluid. Sequestrum in neck removed. Rubber drain. Traction	Had another incision and drainage 8 mos. later, rubber drains inserted	Staphylococcus aureus / 3½ yrs.	X-ray shows some destruction of femoral head, and slight shortening of neck 3	No complaints. Walks miles and plays all games without handicap 4	Flexion 75, extension 175, abduction 30, adduction 5, external rotation 20, internal rotation 0. Slight limp 2
32. S.L. M 14 yrs.	Hip, R. / 14	Furuncle 6 wks. ago. T. ? W.B.C. 12,000, 74%	Ilium. Pre-operation	Anterior incision. Thin gray pus under tension. Rubber tube drain into joint. Bone not entered	2 subsequent operations, posterior incision at third operation. Rubber dam drain	Staphylococcus aureus / 4 yrs.	¾ inch short. X-ray shows osteophytes at acetabulum and some destruction of femoral head 2	No symptoms. Hip is just as good as other, but both show poor motion due to congenital spastic paraplegia 4	Motion in hip as good as on opposite side. Reduced because of muscle spasticity 3
33. Z.O. F 3 yrs.	Hip, L. / 200?	Injured hip 8 mos. ago, put into spica at another hospital. Diarrhœa 2 wks. ago. T. 103 W.B.C. 29,000, 93%	Femoral head. Pre-operation	Anterior and posterior incisions. 500 c.cm. of foul pus, burrowed into pelvis and thigh. Rubber dam drains and gauze packs. Traction	2 subsequent operations to drain soft tissue abscesses and to open fæcal fistula into pelvic abscess	Non-hæmolytic streptococcus and bacillus coli / 11½ yrs.	Hip became ankylosed in bad position, requiring subtrochanteric osteotomy later 0	No symptoms. No recurrences. Fæcal fistula cured 4	Bony ankylosis. 0
34. H.S. M 6 mos.	Hip, R. / 14	T. 102 W.B.C. 13,000, 50%	Head, neck, and upper ⅓ of shaft of femur. Pre-operation	Posterior incision. 30 c.cm. thin purulent fluid. Bone not incised. Rubber dam drain into joint	2nd incision and drainage 20 days later because of fever. No pus found in femur. Rubber dam drains	"Streptococcus" / 3 yrs.	X-ray shows some previous destruction of head, now repaired. No shortening. 10 degree flexion deformity 3	No symptoms. Active, healthy child, walks and runs without limp or handicap 4	Hip stable. Motion normal except for the 10 degrees' limitation of extension. No limp or spasm 3
35. R.T. F 2 yrs.	Hip, R. / 60	Bronchitis? T. 104 W.B.C. 23,000, 85%	Femoral head necrotic and dislocated on admission	Posterior incision. 50 c.cm. thick pus. No note about reducing head. Rubber dam drain. Traction	Necrotic head and neck removed at 2nd operation. Bifurcation operation years later, then hip fusion for instability	"Streptococcus" / 12½ yrs.	Hip ankylosed following hip fusion operation. 2 in. short 0	No symptoms since hip fusion. No recurrence of infection. Hip in good position. Moderate limp due to shortening 3	Bony ankylosis 0
36. W.Y. M 10 yrs.	Hip, L. / 17	2 furuncles. Struck by auto. T. 103 W.B.C. 20,000, 80%	Upper ⅓ of femur on admission	Posterior drainage. Rubber tube sewed into joint. 3 oz. thick pus. Traction	Sequestrectomy of head and neck of femur 20 days later. Hip stabilization operation after 3 yrs.	Staphylococcus aureus / 10½ yrs.	X-ray shows almost complete loss of head and neck. 1¾ inches shortening. 10 degree flexion deformity. 2 inches atrophy of thigh 1	Has had a recent recurrence of the infection in hip, necessitating operation. Sinus closed at present. No pain 2	Hip shows practically no motion. Fibrous ankylosis 0

In order to clarify the study, the cases have been divided into three groups, as follows:

Group 1 consists of 22 cases which were bacteriologically proved and which were not complicated by bone infection. This group constitutes the main series upon which this study is based.

Group 2 consists of 4 cases similar in every way to the above except that they were not bacteriologically proved.

Group 3 consists of 10 cases, all proved bacteriologically but which were complicated by osteomyelitis at the joint.

Group 1

Twenty-two cases, bacteriologically proved, uncomplicated.

Incidence. There were 5 females and 17 males, a ratio of 1 to 3.4. Age at operation ranged from 6 months to 14 years (except for one male of 32), averaging 6.5 years. The disease is thus essentially one of childhood.

The hip was affected in 10 cases, or 45.5 per cent; the knee in 6, or 27 per cent. There were 3 elbows, 2 ankles, and 1 shoulder.

Etiology. With one exception (Case 11, Table I), all the infections in this group were of metastatic, hæmatogenous origin. The etiology of such infections can rarely be definitely established. A history of definite trauma was obtained from 5 patients, and in 15, or 68 per cent of the group, there was evidence of foci of infection which might have had a causal relationship. Only two patients had neither focus of infection nor trauma. The foci of infection encountered, in the order of their frequency, were: infected tonsils, chronic osteomyelitis in a distant bone (i.e., a bone not entering into the formation of the affected joint), otitis media, pyelitis, septicæmia, purulent cervical adenitis, pneumonia.

Symptoms and physical signs did not differ, in this series, from the usual textbook descriptions. The most constant symptoms were pain and inability to use the affected joint, with swelling in all cases except some of those in which the hip was affected. Varying degrees of general reaction were present, from high fever and prostration to moderate pyrexia and malaise. The *duration of symptoms* before operation varied between 2 and 28 days, averaging 9 days. Often the patient had been treated at home, during these important days, without a correct diagnosis.

The temperature per rectum ranged from 99.4 to 105 degrees F., the mean temperature on admission being 102 degrees. The white blood cell count was listed as low as 6,800 and as high as 52,800, with a mean of 16,800. The mean percentage of polymorphonuclear leucocytes was 72.0 per cent.

Roentgenograms strongly suggested pyarthrosis in 9 cases; in 7 cases the evidence from this source was less helpful, while 6 patients had no preoperative roentgenogram.

Diagnosis. This is more difficult than one is led to believe. Especially is there difficulty in the differential diagnosis between this condition and (a) joint tuberculosis, (b) acute rheumatic fever, (c) sympathetic sterile effusion into a joint near infected area, as osteomyelitis or cellulitis, (d) acute non-suppurative infectious synovitis.

There is no single test for joint suppuration. The history, physical examination, clinical laboratory reports, and roentgenograms must all be carefully studied, and observation in the hospital for a day or two may be necessary to arrive at a diagnosis. It is probably less serious to open a sterile joint than to fail to open a purulent one, although in the presence of surrounding inflammation the most acute surgical judgment is needed to make such a decision. *Aspiration* of the exudate for the purpose of diagnosis is invaluable. This should be performed in every case in which there is any doubt about the diagnosis, smears and cultures being made immediately; even if both of these are negative, however, arthrotomy should be performed if the clinical and roentgenographic signs are sufficiently suggestive of suppuration.

The positive diagnosis of pyarthrosis cannot be made in the early stages from the roentgenogram alone; but when an effusion, the density of which is consistent with pus, is seen in a joint having the necessary history and physical signs, that diagnosis is strongly suggested.

Operation. In 20 patients of Group 1 the purulent joint was treated by wide arthrotomy, and a drain was placed into the joint cavity in each case, to ensure continued evacuation of the pus. The material used for these intracapsular drains was soft rubber dam or soft goiter tubing; heavy walled rubber tubes were placed down to capsule when necessary to preserve a drainage tract through thick muscle layers, as at the hip. All drains were usually sutured in place. At the knee, the rubber dam drain was often placed completely through the joint, traversing the suprapatellar pouch.

Incisions were placed in dependent situations when the anatomy of the joint made this feasible; e.g., posteriorly at the hip (except in 2 cases) and shoulder, posterolaterally at the elbow; at the knee, two longitudinal incisions were made, one on each side of the patella.

In the 2 remaining joints of Group 1, arthrotomy was not performed for the reason that the diagnostic aspiration of pus was followed by rapid, unexpected, and complete resolution of the infection. They were undoubtedly infections with attenuated organisms: one an elbow from which Staphylococcus aureus was cultured, the other a pneumococcic infection of the knee (Cases 19 and 22). The diagnostic paracentesis had no such effect in the remaining cases.

Pathology. Every joint in this series was a definitely purulent one when opened. In all cases pus was encountered, varying in consistency from thin gray seropurulent exudate to thick, yellow, creamy pus. The synovial membrane was usually severely injected and hypertrophied, with more or less necrosis; the capsule and periarticular structures were usually described as œdematous. Granulation tissue in many instances encroached upon the articular cartilage, but in every case in this group, in which the operative note described it, the cartilage itself was said to be intact.

In no case in Group 1 was there any destruction of bone, either before the arthrotomy or subsequent to it. Nor was there any case of phlegmon extending from the joint through the fascial planes of the extremity.

Microscopic sections were made in only 6 cases. It has been the feeling in this hospital that the arthrotomy in a purulent joint should be done as quickly as possible, with no unnecessary opening up of new tissue spaces to the infection. Hence the paucity of material for microscopic study. The sections which were made confirm the already well known pathological picture: a synovial membrane thickened by œdema, hypertrophy, and hyperplasia, these processes extending also into the subsynovial areolar tissues to varying extents; synovial membrane and underlying tissue densely infiltrated with polymorphonuclear leucocytes, and more or less extensive necrosis of the superficial layers of synovial membrane.

Bacteriology. Positive cultures were obtained from all the joints in Group 1. The organisms encountered, in the order of their frequency, were:

	Cases	Per cent
Staphylococcus aureus	7	32
Hæmolytic streptococcus	4	18
Non-hæmolytic streptococcus	3	14
Staphylococcus plus streptococcus	3	14
Pneumococcus	3	14
"Staphylococcus" (variety not stated)	1	4.5
Bacillus pyocyaneus	1	4.5

The Bacillus pyocyaneus is not common in this disease; in this case an operation on the prepatellar region, performed at another hospital, resulted in a Bacillus pyocyaneus infection, and the patient was brought to us after the knee became involved (Case 11).

The virulence of these organisms and the results obtained in joints infected with each, will be discussed presently.

Complications. The complications usually spoken of in treatises on acute suppurative arthritis are septicæmia, osteomyelitis, phlegmon, ankylosis, amputation, death. None of these untoward events occurred in any case in Groups 1 and 2 of this series. One patient (Case 21), with a purulent shoulder, had several recurrences requiring arthrotomy; another had a pathological dislocation of the hip. There were no other serious complications.

Postoperative treatment. Motion. Gentle *passive* motion was instituted immediately after the operation, and this was replaced by *active* motion as quickly as the patient was able to bear it. The average time at which active motion was begun was 2.5 days after operation, although records of this were not kept on all of the charts. In 2 cases (12 and 14) the arthrotomized knee had to be moved under anæsthesia at 6 weeks and 12 days, respectively, because of stiffness. Both of these patients obtained good, but not excellent, results.

Removal of drains depended upon the decrease in drainage and the patient's temperature. The rule was gradually to withdraw the drain as fast as the subsidence of the infection would allow. Complete removal usually occurred between the seventh and twenty-first days, though it varied between the first and the fortieth days after operation. Dakin irrigations were used in 1 case.

Traction was used in 10 of the 18 cases of lower extremity involvement; 8 hips and 2 knees were thus treated. No figures were available as to how long the traction was maintained.

Weight-bearing was not forced. The earliest day on which walking was begun in a lower extremity case was the twenty-eighth day after operation, and the average was 45 days. The date was determined by the general condition of the patient and the appearance of the joint.

Results of the operations. All but 9 of the patients were seen and examined by the authors in the follow-up clinic, and their condition at the time determined as accurately as possible. When it was impossible to get a patient in for examination, his condition was estimated from the most recent notes on his history.

The length of time elapsed between operation and final follow-up examination for this group averaged 4.3 years, there being only 1 case with a

follow-up of less than 1 year, and the longest period being 14 years.

The result of the treatment in each case was evaluated according to the anatomical, symptomatic, and functional condition of the joint at the time of last examination; the degree of success obtained by the operation was indicated numerically from 0 to 4 in each of the named categories of anatomy, symptoms, and function: 0, representing a failure; 1, a poor result; 2, fair; 3, good; and 4, an excellent result. This system of follow-up evaluation was originated at the Presbyterian Hospital in New York City in 1914, and was described in *The Medical and Surgical Reports* of that institution in 1918, by Dr. James A. Corscaden. According to this system an excellent result is designated an anatomical 4, symptomatic 4, functional 4, or more simply as 4–4–4; a complete failure would be 0–0–0. A patient who had a good anatomical, excellent symptomatic, but poor functional result would be classed 3–4–1.

In estimating the anatomical result of the operations, account was taken of such variations from the normal as shortening, atrophy, bone destruction, relaxation, subluxation, dislocation, flexion deformity, and ankylosis. For the symptomatic result, the patient's complaints of pain, stiffness, limp, and fatigue were weighed. To determine the functional or economic result, a careful study was made of the exact range of motion at the joint, these measurements being made personally by the authors in most of the cases; also the gait, the handicap in work or athletics, the ability to execute skilled movements were studied.

The personal judgment of the authors was necessarily called into play in arriving at the numerical classification of these cases, particularly of those not examined personally in the follow-up clinic. If there was any difficulty in estimating any phase of a result, the classification was purposely made to err toward the lower rating. If ankylosis occurred in any joint, it was considered an anatomical as well as a functional failure. Table I gives a short résumé of every case in the series, with its anatomical, symptomatic, and functional result and the numerical classification.

Of the 22 patients in Group 1, there were 12, or 54 per cent, in whom the anatomical, symptomatic, and functional results were all excellent; i.e., 4–4–4 results, or joints restored practically to normal. These patients have little if any residual of the disease apparent in the roentgenogram, no pain, stiffness, or limp, and no limitation of motion or activity.

In addition to these 12 excellent results, there were 5, or 23 per cent, in whom *good* results were obtained, viz.: one 3–4–4, two 3–4–3's, one 3–3–3, one 2–4–4. One result was fair, a 3–4–2, and 2, or 9 per cent of the group, were listed as poor; one of the latter was a 0–0–0 because of a pathological dislocation which the patient refused to have treated (Case 5), and the other was a 3–0–0, a patient with numerous recurrences, who finally disappeared, still in need of another operation (Case 21).

Two patients in this group could not be classified because of insufficient data.

The average duration of symptoms before operation in the excellent results was 7.5 days, the majority being less than 5 days; for the good and fair results the average was 12 days. The one poor result in which the duration was certain had had symptoms for only 3 days.

The postoperative temperature reached normal in from 4 to 33 days, averaging 15. The average time required for the healing of the wounds was 48 days.

Group 2

Four cases, not proved bacteriologically, uncomplicated.

These cases differ from those in Group 1 in no way except that the causative bacterium was not determined. In 3, cultures were taken at the time of arthrotomy and no growth occurred; in the other, there is no record of a culture having reached the laboratory. Clinically and pathologically they were typical cases of acute suppurative arthritis without involvement of the bone.

The mean temperature and blood count, and the operative procedure were approximately the same as in the previous group. Drains were used in each case, and in each joint pus was found. The follow-up averaged 7.7 years, ranging between 5 and 11 years. Two hips and two knees were involved.

The outcome in these cases was 4–4–4 in 2, 0–4–0 in 1, and 1–0–1 in 1; or, two excellent and two poor results.

Group 3

Ten cases, bacteriologically proved, with bone involvement.

The hip was the joint affected in every case in this group. The bone infection was an acute osteomyelitis of the femur or acetabulum or both, present at the time of admission to the hospital; in no case was there a focus of chronic osteomyelitis in another bone.

TABLE II.—END-RESULTS ACCORDING TO GROUPS

End Result	Group 1	Group 2	Group 3
4–4–4	12	2	..
3–4–4	1	..	..
3–4–3	2	..	2
3–4–2	1	..	1
3–3–3	1	..	..
2–4–4	1	..	..
2–4–3	..	..	1
2–3–2	..	..	1
1–2–0	..	..	1
0–4–0	..	1	2
0–3–0	..	..	1
3–0–0	1	..	..
0–2–0	1	..	1
Unclassifiable	2	1	..
Total No. of Cases	22	4	10

The average age of this group was 5.7 years, and the average duration of symptoms before operation was 49 days (in Group 1 it was 9 days), exclusive of one patient who had been treated in another hospital in a spica, without operation, for 200 days.

Symptoms, physical signs, temperature, and blood counts did not differ materially from the cases in Group 1.

The causative organisms were: staphylococcus in 4 cases, streptococcus in 4, mixed staphylococcus and streptococcus in 1, and mixed streptococcus and Bacillus coli in 1.

The arthrotomy and insertion of drain in this group had to be followed in all but 2 cases by subsequent operations for the removal of sequestra, partial ostectomy, or to widen the drainage tract. Hence the pathology and the postoperative course were somewhat different from the cases in Group 1. It was impossible to say whether the osteomyelitis or the arthritis was the original lesion in these cases; there is little doubt, however, that an undiagnosed, untreated pyarthrosis at the hip could be expected to cause bone infection sooner or later.

Traction was used in 6 of these cases, and a plaster spica in 1. Attempts to establish motion met with much less success than in the uncomplicated cases. The removal of drains, healing of sinuses, and length of stay in bed were determined by the progress of the osteomyelitis rather than by the joint infection.

The follow-up period for this group averaged 7 years. Among the 10 cases there were no excellent results, although 6 patients were completely relieved of symptoms; 4 results may be called good (Cases 30, 31, 32, 34), 1 poor (Case 28), while 5 were failures. Four of the failures were due to ankylosis, 1 to an irreducible dislocation which was present on admission. There were no deaths, amputations, or cases of septicæmia; the one phlegmonous abscess was present on admission in the patient (Case 33) who had lain 200 days in a spica in another hospital, and was undoubtedly due to the long delayed operation.

Thus 50 per cent of the cases in this group resulted in failures, with no excellent results. When the outcome of these cases is compared with that of the cases in Group 1, it is seen that the presence of bone infection as a complication of purulent arthritis greatly increases the seriousness of the disease, and renders the prognosis for function much less sanguine. Table II shows graphically the results in each group.

FACTORS INFLUENCING FINAL RESULTS

The results of the treatment in this series of cases are surprisingly good when compared with the case reports in the literature. The factors which may have some bearing on this difference will be discussed under the following headings:

1. *Virulence of the infection.* There were, of course, wide variations in the virulence of the infecting bacteria, as is shown by the fact that one patient with a Staphylococcus aureus infection of the knee recovered after simple aspiration, whereas others with the same organism were prostrated with a very severe infection and ended with poor joints in spite of early and efficient treatment. Low virulence of the bacteria may account for some of the excellent results obtained in this series, but that it cannot account for all of them will be evident to one who studies the figures for temperature and blood counts given in Table I. It may not be unusual to see a joint infected with the pneumococcus get well with aspiration, but this must certainly be an unusual event with the staphylococcus. The authors cannot speak with experience about the result of aspiration as the sole method of treating streptococcus pyarthroses. Table III shows the end-results of the cases in Group 1 arranged according to the infecting organism.

2. *Early diagnosis and arthrotomy.* There was little temporizing with purulent joints in this series. Arthrotomy was performed in each case as soon as was feasible after the diagnosis was made. The only delay was in the patient's getting to the hospital. The best results, in general, were obtained in those joints which had early diagnosis and early arthrotomy.

3. *The use of drains.* Far from constituting a misdemeanor, it is believed that the results in this series of cases will show that the use of soft rubber drains into the joint cavity is one of the most helpful adjuncts in the treatment of pyogenic joints.

TABLE III.—END-RESULTS IN GROUP I ACCORDING TO INFECTING ORGANISM

Result	4–4–4	3–4–4	3–4–3	3–4–2	3–3–3	2–4–4	3–0–0	0–2–0	Unclassifiable	Total No. of cases
Staphylococcus aureus	4		1				1		2	8
Hæmolytic streptococcus		1		1	1			1		4
Non-hæmolytic streptococcus	1		1			1				3
Streptococcus and staphylococcus	3									3
Pneumococcus	3									3
Bacillus pyocyaneus	1									1

TABLE IV.—END-RESULTS IN GROUP I ACCORDING TO DURATION OF SYMPTOMS BEFORE OPERATION

	Duration of symptoms in days																							
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25 plus
4–4–4	2	3	1		1		1		1					1						1					1
3–4–4									1																
3–4–3						1								1											
3–4–2		1																							
3–3–3																									1
2–4–4														1											
3–0–0		1																							
Unclass.			1																		1				

In one case, the duration of symptoms was unknown.

The drains must be soft, they must not be large enough to cause pressure necrosis, and they should be withdrawn as rapidly after operation as the subsiding of the infection will permit.

4. *Traction.* It is believed that the routine use of traction in these cases has exerted a favorable influence. Traction helps to relieve pain, to prevent or overcome flexion deformities, and possibly to protect the articular cartilages if, as Phemister claimed, necrosis of this tissue first occurs at points of pressure in a suppurating joint. The traction apparatus must be so applied that it will not interfere with free motion at the joint. The simplest method is by means of an anklet and a weight over a pulley at the end of the bed.

5. *Motion.* A great deal has been written in the literature about active versus passive motion, much to the discredit of the latter. It would be ideal treatment in pyogenic joints to start frequent, prolonged, and complete active motion immediately after operation, but such treatment can be attained only in rare instances. One needs only to see a single case to appreciate the suffering undergone by a patient with such a lesion, and when the average age of these patients is recalled, it becomes obvious that too much cannot be expected of active motion.

Passive motion, extremely gentle in its application, never forced in its degree, repeated several times a day by the surgeon, is much more feasible, and almost if not quite as effective as active motion in the early postoperative treatment. Each joint in this series was thus treated, and active motion substituted for passive as soon as possible. Emphasis must be placed on the *gentleness* of this passive motion. The importance of active motion cannot be overemphasized, but at the same time the usefulness of passive motion should not be overlooked.

6. *The main purpose* in the treatment of acute suppurative arthritis is, of course, the evacuation of the pus by the most efficient means possible. The use of drains and of early passive and active motion was invaluable in accomplishing this in the present series of cases, and the fact that these methods, when correctly used, are not destructive to infected joints is demonstrated by the end-results here reported.

SUMMARY AND CONCLUSIONS

1. An historical review of the treatment of acute suppurative arthritis is presented.

2. Case reports of this disease are scarce in the literature, the results reported are usually bad,

and the attitude of the writers toward the disease is gloomy.

3. The idea of attempting to preserve the function of a purulent joint is relatively recent and is not yet widespread.

4. Thirty-six cases of acute suppurative arthritis are presented, in which operations had been performed at the New York Orthopaedic Dispensary and Hospital during the past 15 years.

5. Twenty-two of these cases were bacteriologically proved and uncomplicated by bone infection. The end-results in this group were: 12, or 54 per cent, were excellent anatomically, symptomatically, and functionally; 5, or 23 per cent, were good; 1 was fair, and 2, or 9 per cent, were poor.

6. Four cases were similar to the above except that they were not bacteriologically proved. Results in this group were, 2 excellent and 2 poor.

7. Ten cases were complicated by infection of the bone at the joint. The results in these were much worse than in the above groups, there being no excellent results, and five failures due to ankylosis or dislocation.

8. It is thus seen that the presence of bone destruction greatly increases the seriousness of this disease.

9. The average follow-up period was 6.5 years. The average age at operation was 6.5 years. There were thrice as many males as females. The hip was involved in 22 cases, the knee in 8; there were 3 elbows, 2 ankles, 1 shoulder.

10. The staphylococcus was the infecting organism in 12 cases, streptococcus in 11, mixed staphylococcus and streptococcus in 4, pneumococcus in 3, mixed streptococcus and Bacillus coli in 1, Bacillus pyocyaneus in 1.

11. In general, the best results were obtained in those joints which had early diagnosis and early evacuation of the pus.

12. Active postoperative motion cannot be depended upon as the sole method of continuous evacuation of pus from an infected joint, because of the extreme pain and the usually tender age of the patient.

13. In obtaining efficient continued drainage, in this series of cases, the most useful adjuncts to arthrotomy were found to be the insertion of soft rubber drains into the joint cavity and gentle passive motion immediately following the operation. The importance of *active* motion after arthrotomy cannot be overestimated, and this was substituted for passive motion as soon as the patients could stand it.

14. There were no deaths, no amputations, no septicæmias; ankylosis occurred only in 4 cases in which bone destruction at the hip had occurred before operation.

15. The prognosis for function in acute suppurative arthritis is good if the diagnosis is made early and this is promptly followed by arthrotomy and drainage. It is poor if treatment is delayed until bone destruction has taken place.

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SUBTOTAL VERSUS TOTAL HYSTERECTOMY

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THE recent literature concerning hysterectomy for non-malignant pelvic conditions shows a definite trend of opinion toward the employment of the total rather than the subtotal or supravaginal operation. This tendency seems to be due largely to emphasis on the possibility of subsequent development of cancer in the stump of the cervix uteri, though the more radical operation has also been recommended for the relief of cervicitis alone. As apparent justification for this position, a majority of the reports seen by us during the last 5 years show very little or even no greater mortality with total than with subtotal hysterectomy (Table I).

TABLE I.—MORTALITY IN TOTAL VERSUS SUBTOTAL HYSTERECTOMY

	Subtotal hysterectomy		Total hysterectomy	
	Number	Mortality per cent	Number	Mortality per cent
Masson	217	1.8	229	1.3
Nelson	122	3.2	476	2.9
Fullerton and Faulkner	609	4.4	1,078	4.1
Burch and Burch	166	4.2	32	3.1
Mayo and Mayo	3,085	1.2	1,588	1.8
Greenhill	1,857	4.47	551	4.72
Read and Bill	1,739	2.1	605	3.1
Total	7,795	2.6	4,559	3.0

From the figures in Table I we can calculate 7,795 subtotals with 199 deaths or a mortality rate of 2.6 per cent, and 4,559 totals with 139 deaths or a mortality of 3.0 per cent. However, a critical review of the reports containing these series makes the figures less convincing. The series reported by Mayo and Mayo refers to the hysterectomies for fibroid only which were done at the Mayo Clinic from 1916 to 1929 and includes some of Masson's cases. They believe that in their figures the difference in favor of the subtotal operation may be apparent only because of sampling or the occurrence of graver risks among those selected for the total removal. They further believe that the latter reason also explains the higher mortality for total hysterectomy in other reports. Von Graff expressed the same opinion. Such reasoning is so contrary to usual surgical practice that we are at a loss to explain it, unless the reference is to operation in the presence of infection of the cervix or of malignancy. In fact, it is not uncommon, when a total hysterectomy seems desirable, to be forced to resort to the less formidable subtotal operation on account of poor condition of the patient before or during operation or because of technical difficulties. Read and Bill conclude that subtotal hysterectomy carries less risk "in spite of the fact that it includes those patients who are poor operative risks." Nelson gives as partial explanation for the higher mortality with the supravaginal operation in his series that "it has often been done in poor risks." Moreover, in regard to peritonitis he makes the interesting observation that the danger should be as great in cutting through the infected cervix as through the wall of the vagina which "is more accessible and can be more easily sterilized than the cervix." The exceptionally high mortality for the subtotal operation in the report by Fullerton and Faulkner is unexplained. Similar figures in Greenhill's series were due to the unusually high mortality (8.9 per cent) with subtotal hysterectomy plus bilateral salpingectomy in cases with advanced tubal and ovarian infections involving adhesions to adjoining structures. Where hysterectomy alone was done, the mortality was 5.5 per cent for total and only 0.8 per cent for subtotal. The series of Burch and Burch contains too few totals to be of much significance. With the exception of Fullerton and Faulkner, all authors who mention morbidity and complications show them to be more frequent with total hysterectomy. Fullerton and Faulkner give their incidence of shock, injured viscus, hæmorrhage, etc. as 5.5 per cent for total and 6 per cent for subtotal hysterectomies, the difference (0.5 per cent) in favor of total being reversed if cardiac complications are not included. It might be said also that some, at least, of these statistics were derived from special clinics and therefore cannot be used as a general guide in private practice.

We have undertaken a study of abdominal hysterectomies done at Harper Hospital with the expectation that the figures from this large general hospital might fairly represent the relative results to be expected from the two types of operation in private practice. Our study included

the 5 years from January, 1928, through December, 1932, during which time there were 1,379 abdominal hysterectomies for benign gynecological conditions. This is exclusive of all cases of cervical carcinoma regardless of type of operation. To make the conditions under which the two operations were performed as nearly comparable as possible, we further excluded operations done in the presence of malignancy of the body of the uterus and of the adnexa. Cæsarean sections or ruptured uteri followed by hysterectomy were also not included. It is noteworthy, however, that the inclusion of these eliminated cases (80) would have changed the mortality figures only a fraction of one per cent. Of the 1,376 operations 1,141 were subtotal hysterectomies with 30 deaths and 235 total with 15 deaths —a mortality rate of 2.6 and 6.4 per cent, respectively. The combined mortality rate was 3.3 per cent.

TABLE II.—HARPER HOSPITAL SERIES SHOWING MORTALITY

Year		Number	Per cent	Mortality Per cent
1928	Subtotal	241		2.9
	Total	66	21.5	9.1
1929	Subtotal	238		2.9
	Total	62	20.7	6.5
1930	Subtotal	237		3.8
	Total	34	12.5	2.9
1931	Subtotal	220		2.3
	Total	34	13.4	5.8
1932	Subtotal	205		1.0
	Total	39	16.0	5.1
	Subtotal	1,141		2.6
	Total	235	17.0	6.4

Table II gives the number of both operations with their mortality rates for each year. It also shows the yearly percentages of total hysterectomies. The mortality rates for the subtotal operation have remained at a fairly constant level whereas those for the total have tended to diminish. In addition, it is seen that the years with the lower percentages of total hysterectomy had a somewhat lower mortality rate for that operation. On the assumption that possibly the lower rates were due to a tendency to elect the subtotal operation for poor risks, the years 1929 and 1931 were studied. In 1929, the total operation was done on 11 poor risks (hæmoglobin below 70 per cent, cardiac disease, nephritis, diabetes), and in 1931 on 10. The subtotal operation was performed on 32 in poor condition in 1929 and 38 in 1931. Because of the small yearly number of cases, we consider these figures as merely suggestive.

It has been stated in the literature that the apparent advantages in mortality of subtotal over total hysterectomy varied with the skill and experience of the operator, the inference being that the more experienced operators could obtain as low mortality rates with total as subtotal hysterectomy. To test this assertion we investigated the whole group of 235 total operations, and for comparison the 458 subtotals done in 1929 and 1931. The years 1929 and 1931 were selected as being at neither extreme of time and therefore probably representative, the mortality rate, moreover, for these periods being the same as for the whole group of subtotal hysterectomies. We found that the 693 operations (total and subtotal) had been done by 46 different gynecologists and general surgeons of greatly different experience as evidenced by the number of hysterectomies performed by each. Two operators did 50 or more during these periods; five, 25 or more and less than 50; thirty-eight, less than 25. Table III shows the comparative mortality rates for these groups. A separate classification was given the clinic cases as these were in large part operated upon by a series of five residents, though under the supervision and usually with the assistance of a senior attending gynecologist. Besides demonstrating the value of experience, this table shows a lower mortality for subtotal hysterectomy in every division, and except in the clinic cases the difference is striking.

TABLE III.—COMPARATIVE MORTALITY OF DIFFERENT OPERATORS

Cases per operator	Subtotal hysterectomy Mortality per cent	Total hysterectomy Mortality per cent	All cases Mortality per cent
50 plus	0.7	4.3	2.2
25 to 49	0.9	4.3	1.9
1 to 24	4.8	11.9	6.6
Clinic	4.8	5.4	5.1

The immediate causes of death with the actual numbers for both subtotal and total hysterectomy are shown in Table IV. In general these figures confirm those usually given except for the higher incidence of infection and peritonitis in our series. The percentage occurrence of these causes was approximately 57 per cent of the subtotal and 73 per cent of the total hysterectomy deaths, or mortality rates of 1.5 per cent and 4.7 per cent, respectively, from these causes alone. Embolus caused deaths in 0.5 per cent with the subtotal

and 0.8 per cent with the total operation. Shock with myocardial failure resulted fatally in 0.4 per cent and 0.8 per cent of the 1,141 subtotal and 235 total hysterectomies. These statistics show that the usual causes of death (peritonitis, embolus, and shock) were common to both types of operation, but occurred to a greater degree in total hysterectomy.

TABLE IV.—IMMEDIATE CAUSES OF DEATH

	Peritonitis and infection	Embolus	Shock and myocardial failure	Diabetes	Pneumonia	Total
Deaths in 1,141 subtotal hysterectomies	17	6	5	1	1	30
Deaths in 235 total hysterectomies	11	2	2	0	0	15

The influence of accessory procedures at the time of operation was studied in the groups mentioned in Table IV, viz., the 235 totals for all 5 years as compared to the 458 subtotal hysterectomies for the years 1929 and 1931. Removal of the uterus without the adnexa resulted in 1 death in 66 totals and 5 deaths in 174 subtotals—a mortality rate of 1.5 per cent and 2.9 per cent, respectively. With salpingectomy or salpingo-oophorectomy the results were quite different, for with the 147 totals there were 13 deaths (8.8 per cent) and with the 247 subtotals there were 7 deaths (2.8 per cent). Of the 147 totals with salpingectomy or salpingo-oophorectomy there were 80 with definite clinical and laboratory evidence of pelvic inflammation such as extensive adhesions or subacute or chronic salpingitis. The mortality was 10 per cent. In 67 cases with no note of pelvic inflammation there was a mortality of 7.4 per cent. Among the 247 subtotal hysterectomies with the same accessory procedures there were 165 showing pelvic inflammation and 82 without, the mortality being 3 and 2.4 per cent, respectively. It is probable that many cases designated by us as without pelvic inflammation were actually complicated by the condition although it was not so stated in the histories. It is quite evident that the higher mortality of hysterectomy plus salpingectomy and salpingo-oophorectomy was due in part, at least, to difficulties encountered because of pelvic inflammation as was noted also by Greenhill. This observation is supported by the mortality rates of subtotal and total hysterectomy for fibroid with and without pelvic inflammation as shown in Table V.

Of other accessory procedures, appendectomy was the most frequent, being done in 83, or 35.3 per cent, of the totals and in 220, or 48 per cent, of the subtotals. Three of the patients in whom total hysterectomy plus appendectomy were done died, a mortality rate of 3.6 per cent as compared to 6.4 per cent for the whole group. There were no deaths among the subtotal cases with appendectomy. We believe these results should not necessarily be interpreted as indicating that removal of the appendix added no danger to hysterectomy, but rather that appendectomy was reserved in general for the more favorable cases. Supporting the latter possibility, and without taking into account technical difficulties, etc., is the fact that among the totals with appendectomy there were 8.4 per cent poor or questionable surgical risks (hæmoglobin below 70 per cent, cardiac disease, nephritis, diabetes) as compared to 19.1 per cent for those without appendectomy. Among the subtotal hysterectomies plus appendectomy there were 10.9 per cent poor risks as compared to 19 per cent for the remainder of those done in 1929 and 1931. Other accessory operations such as perineorrhaphy, colporrhaphy, cholecystectomy, and herniorrhaphy were performed in an additional 21 of the totals and 35 of the subtotals—with 1 death among the totals.

TABLE V.—MORTALITY WITH AND WITHOUT PELVIC INFLAMMATION

	Subtotal Mortality per cent	Total Mortality per cent
Hysterectomy for fibroids without pelvic inflammation	2.8	3.8
Hysterectomy for fibroids with pelvic inflammation	3.1	19.9
With and without pelvic inflammation	2.9	7.0

DISCUSSION

Our investigations indicate a definitely higher mortality for total hysterectomy than for the subtotal operation. Furthermore, we believe that statements in the literature to the contrary are not convincing when the data on which they are based are analyzed. On the other hand, it seems that when hysterectomy is to be undertaken and there is also a definite indication for removal of the cervix, the more radical operation is not unduly dangerous in the best operative risks.

The actual incidence of carcinoma developing in the cervix after subtotal hysterectomy is not known, but the possibility is worthy of consideration. Polak estimated the occurrence at 2 per cent, a figure which would possibly justify the frequent employment of total operation. But, this is far higher than that stated by other

writers. Von Graff quotes Hochmann as giving 0.27 per cent. Mayo and Mayo reported 99 cases seen at the Mayo clinic from January, 1910, to July, 1930, only 15 of these, however, being in women who had been operated on there. They believe the low incidence in their own cases was due to coning out the cervical canal from above. This procedure may well be of some importance, but it does not remove the usual site of cervicitis and carcinoma of the cervix—the region of the external os. Of much greater value, we think, is their suggestion that following subtotal hysterectomy the cervix be removed later from below or that enucleation of the cervical canal or cauterization be carried out. In several instances where total hysterectomy seemed indicated but was not done on account of the patient's condition, one of us has later removed the stump of the cervix without difficulty, but this has the obvious objection of additional hospitalization. In cases in which the cervix is torn and infected but not sufficiently so to make its removal imperative, thorough cauterization or conization under anæsthesia before the abdominal incision is made should accomplish much in preventing carcinoma in the cervical stump. Moreover, the rare, very early, and therefore local and unrecognized carcinoma would almost certainly be destroyed. In our series the operation records of the 458 subtotals done in 1929 and 1931 showed only 16 of these accessory operations on the cervix, though probably some cauterizations were done later because of persistent leucorrhœa.

SUMMARY

Although there is a definite tendency in the recent literature to ascribe to total hysterectomy a mortality comparable with that of the subtotal operation, a critical study of the reports leaves one far from convinced. In our 5 year series there were 1,376 abdominal hysterectomies (excluding malignancy, cæsarean section followed by removal of the uterus, and ruptured uterus) of which 1,141 were subtotal and 235 total with mortality rates of 2.6 per cent and 6.4 per cent, respectively. There was a tendency for the total hysterectomy mortality to be lower in the years with a relatively smaller proportion of the more radical operation. All groups made on the basis of surgical experience of the operator (number of operations per operator) showed an advantage in mortality for subtotal hysterectomy. Pelvic inflammatory disease made hysterectomy more dangerous and explained in part, at least, the higher mortality of hysterectomy with removal of the adnexa. With accessory operations such as appendectomy and perineorrhaphy, the lower mortality was apparently associated with a selection of the better risks for these additional procedures. The danger of carcinoma developing in the stump of the cervix after subtotal hysterectomy is seemingly not sufficiently great to justify the additional risk of the total operation in any but a small proportion of cases. Other less dangerous procedures should be more frequently recommended.

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DIVERTICULA OF THE STOMACH

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ANATOMICALLY, the term, "diverticulum," is applied to a blind tubular process and pathologically, to any malformation having this character. Akerlund described gastric diverticula as rounded, pocket-shaped, or bag-shaped protrusions from the lumen of the stomach. Thus, broadly speaking, the term includes not only true diverticula, whether congenital or acquired, but also diverticular formations resulting from intrinsic lesions of the gastric wall, such as ulcer or neoplasm. In this paper only true diverticula will be considered in detail.

Diverticula occur in the stomach less commonly than in other portions of the alimentary tract with the possible exception of the jejunoileal region. Fraser stated that these lesions occur in the different parts of the alimentary tract in the following order of frequency: colon, rectum, duodenum, pharynx and œsophagus, stomach, jejunoileum. The statistics of Larimore and Graham are in accord with this statement. In a series of 3,446 examinations of the digestive tract with the opaque meal they found 105 diverticula; 71 were in the colon, 19 in the duodenum, 9 in the œsophagus, 3 in the stomach, and 3 in the jejunum.

The first case of diverticulum of the stomach was reported by Helmont in 1804. Since that time we have found 108 cases, either mentioned or reported in detail in the literature. As might be expected, most of these have been reported since roentgenological examination has become available in diagnosis. Many of the cases reported have not been confirmed at operation or necropsy. This detracts materially from the reliability of the reports because of the difficulty in distinguishing, roentgenologically, true gastric diverticula from false diverticular formations. Our series includes 14 proved cases of diverticula of the stomach.

Four of the specimens of diverticula were obtained at necropsy and 10 were removed at operation. Diverticula of the stomach have been diagnosed roentgenologically in 25 cases at the Mayo Clinic since 1926. In 6 cases of the group, exploratory operations revealed only 2 to be true diverticula; in the 4 others, diverticular protrusions were found to be due to perforating peptic ulcer or to carcinoma. The 19 remaining cases, in which diagnosis was made roentgenologically but not proved or disproved at operation or necropsy, are not included because of the frequent confusion in the roentgenologic diagnosis of these lesions.

CLASSIFICATION

Diverticula of the digestive tract have been variously classified as congenital, or true, acquired or false, and pulsion or traction types. True (congenital) diverticula have been considered to have intact muscular and mucosal layers, whereas false (acquired) diverticula have been considered to be those diverticular formations in which one or more of the mural layers are absent. The terms "pulsion" and "traction" are self-explanatory and have been used frequently in connection with true and false diverticula. Kausch pointed out that the terms "congenital" and "true," and "acquired" and "false" are not always synonymous. Brandes substantiated this statement by reporting a case of an acquired diverticulum in which all layers of the wall of the sac were present.

It is thus evident that there is much confusion and some inaccuracy in the classification of these abnormalities. In order to simplify the subject of gastric diverticula, we suggest the following subdivisions:

1. *True diverticula.* Those in which the pouch includes all coats of the gastric wall without definite evidence that organic disease was the causative factor. Such diverticula probably are congenital (Fig. 1).

2. *Acquired, true diverticula.* In these, all coats of the gastric wall are present although there may be some thinning, and there is evidence that some disease was instrumental in causing the pouching.

(*a*) Pulsion type diverticula result from intragastric pressure which is probably localized.

(*b*) Traction type diverticula are incidental to extragastric adhesions (Fig. 2).

3. *False diverticula or diverticular formations.* In these there is a break in the gastric wall resulting from disease (Fig. 3).

Fig. 1. True diverticulum at the cardiac part of the stomach. The mural elements are intact but are thinned out.

Fig. 2. Acquired true diverticulum of traction type. All layers of the wall of the sac are present, and there is some thinning at the site of the adhesive band.

HYPOTHESES AS TO FORMATION

True diverticula. The etiology of true diverticula is unknown. The question even has been raised as to whether a truly congenital type exists at all. Zahn went so far as to state that no diverticula reported up to 1899 were congenital. Laurell and others expressed the belief that these true diverticula are of the pulsion type and are caused by intra-abdominal pressure among persons with a lax abdominal wall. That this is the true explanation is doubtful, since true diverticula have occurred in young, muscular adults and in children. Gile reported a case of a girl, aged 7, with a diverticulum, and Sinclair one of a 4 months old infant, both being confirmed at operation.

Furthermore, as has been demonstrated by Gianturco and others, intragastric pressure is ordinarily quite low. At the cardia, where most diverticula occur, the pressure is lowest, ranging from 5 to 2 centimeters of water. Alvarez has distended the fresh stomachs of cats and dogs under pressures much greater than those occurring physiologically without producing diverticula. The objection may be raised that this experiment was inadequate, and that continued or repeated pressure would be necessary for the development of diverticula. On the other hand, Fraser consistently produced multiple diverticula in the jejunum by briefly distending this part of the bowel; he thus confirmed his belief that jejunal lesions could be acquired.

Despite views to the contrary, it seems to us that the weight of evidence favors a congenital basis for this group of gastric diverticula. Diverticula are not uncommon in lower animals, especially in the pig. The tip of the fundus in this animal normally develops as a diverticulum. The sloth of South America has a cardiac diverticulum normally (Alvarez). However, the fact that this animal virtually lives in an inverted posture might be interpreted by exponents of the idea as adding weight to the hypothesis that diverticula are acquired by pulsion. The beaver has a projection of the pylorus at the greater curvature of the stomach. The fish Lophius piscatorius, or angler, has protrusions from the pylorus at each curvature and the American aquatic herbivorous mammal, the manatee, has three diverticular compartments, namely, at the pars media, on the greater and lesser curvatures, and at the cardia (Huntington). All ruminants, as well as certain forms of aquatic life, such as the Argyroneta aquatica, Asterias rubens, and others, have similar gastric compartments (Buetschli).

In attempting to explain the occurrence of diverticula of the stomach in man embryologically, Kalbfleisch stated that the fundus of the stomach of man develops as a pouch on the outer side of the cardia. He expressed the belief that, in congenital diverticula, another smaller pouch develops and remains connected with the stomach by a narrow neck. This hypothesis would

Fig. 3. False diverticulum due to weakening of the gastric wall by ulcer.

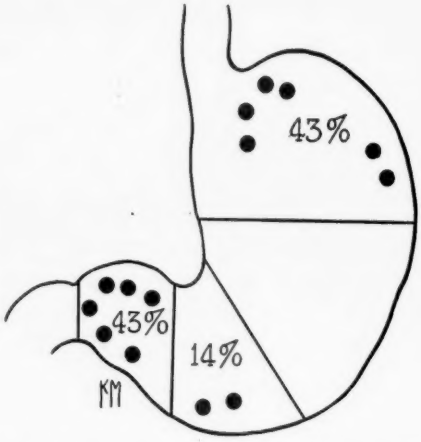

Fig. 4. The situation of the diverticula in our series of cases.

explain only those diverticula that occur at the cardia. It is interesting to note that diverticula of the pyloric region have not infrequently been found in association with aberrant pancreatic tissue. Nauwerck, Falconer, Weischelbaum, Kolb, Wagner, and Gegenbauer found pancreatic tissue in such diverticula. Gile demonstrated heteroplastic colonic mucosa in a gastric diverticulum, and pancreatic tissue adjacent to it.

Anatomically, there is thinning of the circular and oblique muscular fibers at the cardia. Large vessels that enter the gastric wall in this region also contribute to the muscular weakness and make it a site of lowered resistance. Thorel and Zahn believed that this part of the stomach was subject to the greatest strain as food passed along the *Magenstrasse*.

In view of the fact that diverticula of the type under consideration have been found in all regions of the stomach, and almost uniformly present muscular and mucosal elements, which are thin, it seems possible that these diverticula may occur as a result of a congenital localized weakness of the gastric wall. The natural anatomical weakness at the cardia, and the frequent presence of pancreatic tissue at the pylorus, could account for the relative frequency of diverticula at these sites. On the other hand, the thinness of the wall of the sac may be secondary to pressure of gastric contents accumulating in the diverticulum. Such a hypothesis would fit in with the conception that diverticula, as such, exist as vestigial phenomena. It would at least seem reasonable to assume that congenital, anomalous conditions precede development of such an abnormality, if it does not already exist at birth.

Acquired true diverticula. The etiology of this type of diverticulum is usually obvious. Adhesions to the gall bladder, pancreas, and spleen are probably the more common factors producing traction. Jones reported a case in which the gastric wall was adherent to the gastrocolic ligament and colon. Kalbfleisch expressed the belief that this case was probably one of ulcer. Chutro described a case of diverticulum with adhesions to the abdominal wall at the site of a hernia. Von Hansemann reported another case with adhesions to an epigastric tumor. A pulsion diverticulum was caused by a trichobezoar in a case reported by Schulten.

Acquired false diverticula. The gastric wall may be weakened by inflammatory reaction, ulceration, or by neoplasm. It is conceivable that intragastric pressure or progressive ulcerating processes could produce pouching at the site involved.

REVIEW OF MATERIAL IN THIS SERIES

Incidence. Ten specimens in our group were removed in 10 of 11,234 consecutive exploratory operations on the stomach, or 1 in 1,235. Four specimens were obtained in the course of 3,662 routine postmortem examinations, or 1 in 917. Twenty-five roentgenologic diagnoses of gastric diverticulum were made in the course of 91,532 routine roentgenologic examinations of the stomach at the clinic since 1926. As has already been mentioned, many of these were probably not true diverticula.

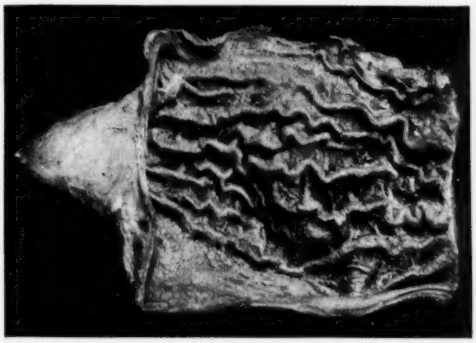

Fig. 5. True cardiac diverticulum specimen obtained at necropsy.

Fig. 6. True diverticulum at the cardiac end of the stomach. Specimen obtained at necropsy with œsophagus intact.

Ages. The ages of the patients in this series ranged from 25 to 59 years; 9 were 40 years of age or older and 5 were from 25 to 40 years of age. The average age was 42 years.

Sex. Diverticula occurred about equally often in either sex; 6 of the patients were men and 8, women.

Situation. The situation of diverticula in cases reported in the literature varies, but they seem to occur most often in the cardia, just below the œsophageal juncture on the posterior wall and usually nearer the lesser than the greater curvature. According to reports they occur next most often at the pylorus, near one or the other curvatures. In our series of proved cases, 6 diverticula were found immediately adjacent to the pylorus, 6 at the cardia, and 2, some distance from the pylorus on the posterior wall (Fig. 4).

Pathologic findings. Diverticula of the stomach in proved cases reported heretofore have varied in diameter from 1 to 5 centimeters. In our group the smallest diverticulum was 1 centimeter in diameter and the largest, 7.5 centimeters (3 inches). The neck of the sac is usually narrow and may or may not be thickened. Grossly, the mucosal and serosal surfaces appear intact. Microscopic examination of sections of the wall of the sac reveal the presence of the mucosal and muscular layers, but these are thinned out. Pancreatic tissue was not found in the diverticulum in any of our cases (Figs. 5, 6, 7, 8). Acquired, or so called false diverticula, may have a deficiency of the mucosal layer or of one or more muscular layers, or both, and the serosa often gives evidence of adhesions to adjacent viscera.

Associated gastric disease. Associated gastric disease was found in 4 of our 14 cases (30 per cent); in 2 cases, there were ulcers adjacent to the diverticula (in 1 case at the cardia, and in the other, at the pylorus), in 1, an adenomyoma in the diverticulum and a duodenal ulcer, and in the remaining case, a sarcoma in the wall of the diverticulum. What part, if any, the adenomyoma and the sarcoma played in the development of the

Fig. 7. Section of wall of true diverticulum. All layers are intact but are thinned out. ×6½.

Fig. 8. Wall of normal stomach adjacent to diverticulum. ×6½.

diverticulum, is problematic. Cleve, Puskepellies, and Nauck considered that such lesions developed in pre-existing diverticula, whereas Bell and Golden doubted whether these should be classed as true diverticula. The literature contains reports of a number of cases with associated disease similar to those in our group. Cleve reported a myoma in a diverticulum, Sandstrom a diverticulum with a benign adenoma, and C. H. Mayo, von Hansemann, Miller, and Mellon, and others, cancerous or precancerous changes in diverticula.

Two or more diverticula in the gastro-intestinal tract. Of the 14 cases included in this report, in 2, demonstrable diverticula were present elsewhere in the digestive tract. In 1 case, multiple diverticula in the colon were found and in another, a duodenal diverticulum was found.

SYMPTOMS

The general opinion of writers on the subject is that most diverticula of the stomach cause no definite symptoms and are usually not of clinical importance. However, some cases have been reported in which there was epigastric distress, positive roentgenologic evidence, and apparent relief following surgical treatment.

In 1 case of our group the patient complained of hæmatemesis, and blood clots were found in the diverticulum. Definite evidence of blood dyscrasia developed later. In 4 cases, part or all of the symptoms may have been attributable to the diverticulum, in 4, the complaint was accounted for by associated gastric or duodenal ulcers, and in 1, a sarcoma may have been responsible for some of the symptoms. Thus in 10 of the 14 cases (71 per cent) symptoms could not be attributed to the diverticulum *per se*. In the 4 cases (excluding the one with hæmorrhage) in which the symptoms may have been related to the diverticula, epigastric pain was present, which might or might not be relieved or aggravated by food, in 2 vomiting had occurred on several occasions (in 1 case probably due to cardiospasm), and in 3 epigastric tenderness was present.

DIAGNOSIS

The recognition of a true gastric diverticulum without the aid of the roentgenogram is impossible, as there is no characteristic clinical syndrome (Fig. 9). Even the roentgenologic findings are difficult to interpret, as is evident from the fact that in 4 of 6 of our cases in which the diagnosis had been diverticula, these diverticula were found at exploration to be false sacs due to malignant disease or to perforating ulcer. The 2 cases in which true diverticula were found were the only cases in our group of proved cases in which the pre-operative diagnosis was correct. Both of these diverticula were at the cardia. However, one is probably justified in making a diagnosis of diverticulum when the roentgenologic findings are consistent and the patient has epigastric distress which is not attributable to other disease.

A number of writers stress the difficulty of roentgenologic diagnosis. Sandstrom said that the diagnosis depends on a niche-like opaque spot surrounded by a defect in the contrast shadow, the appearance of which is also typical of ulceration with surrounding infiltration. Pendergrass outlined the differential diagnosis of diverticulum and hernia through the œsophageal hiatus. He stated that hernias are best seen with the patient in the recumbent Trendelenburg position, and that they are larger during inspiration and smaller during expiration because of variations in intra-abdominal pressure. A gastric diverticulum, on the other hand, does not reveal these changes.

COMPLICATIONS

A complication occurred in but one (7.1 per cent) of our proved cases, in this instance being hæmorrhage. This case has previously been reported by Sutherland. Hæmorrhage also has been reported by Brown, Akerlund, Gile, and by Sinclair.

TREATMENT

The treatment in 10 cases of our series was surgical. The diverticula were removed by local excision, by sleeve resection of the stomach, or by pylorectomy. When gastric or duodenal lesions were associated with diverticula, the surgical procedures were modified according to the type of disease that obtained. The indication for treatment of a diverticulum in the upper portion of the stomach rests on a positive roentgenologic diagnosis plus the presence of epigastric distress not referable to other disease.

Bell and Golden felt that postural drainage should be tried in cases of diverticula at the cardia, as carcinoma has never been reported in this group. They believed that surgery should be performed in all cases in which the lower two-thirds of the stomach was involved, because of the possibility of associated malignant disease and the frequently mistaken roentgenologic diagnosis of diverticula in this region. In the light of the present study, we are led to concur in this opinion. The consensus of opinion favors excision of the sac as the procedure of choice, although inversion of the diverticulum, gastro-enterostomy, and gastric resection have been performed in some instances.

REPORTS OF CASES

SURGICAL

CASE 1. A man, 36 years of age, came to the clinic because of stomach trouble of 3 to 4 years' duration. He complained of a "hot spot" in the upper portion of his abdomen that had been more or less constantly present but had never been aggravated by heavy foods. He made the statement that it felt as though a sac were present near the entrance of the stomach, because there was a dull pain in this region similar to that caused by food packed in the socket of a tooth. Epigastric tenderness was present.

Analysis of gastric contents revealed a total acidity of 60, free hydrochloric acid of 40, and a total quantity of 140 cubic centimeters. The roentgenologic diagnosis was diverticulum of the cardiac end of the stomach. Other findings were irrelevant.

Exploration revealed a diverticulum at the cardia immediately below the œsophagus, passing to the left and along the fundus of the stomach. The diverticulum was excised. The pathologist reported that the diverticulum was 5 by 4 centimeters in diameter, with thinned out muscular and mucosal layers.

One year later the patient reported that he was well.

CASE 2. A woman, 28 years of age, complained of abdominal distress of 12 years' duration. The symptoms had been somewhat indefinite. She stated that the region of maximal distress was situated to the left of, and above, the umbilicus, although pains elsewhere in the abdomen were not infrequent. Belching and alkalies were said to have given relief, whereas food had had no effect on her symptoms unless at times to aggravate them. She occasionally had awakened at night with epigastric pain that usually had radiated to the sternum. She presented the multiple, bizarre complaints so often encountered in neurotic persons.

General physical examination gave negative results. Analysis of gastric contents revealed a total acidity of 44, free hydrochloric acid of 32, and a total quantity of 100 cubic centimeters. The roentgenologic diagnosis was diverticulum on the posterior wall of the cardia.

At operation, a diverticulum was found on the posterior wall of the stomach at the cardia and also an ulcer next to the pylorus. The lesions were excised. The pathologist reported that the diverticulum was 2.5 centimeters in diameter, with an opening into the stomach 1 centimeter wide.

CASE 3. A man, 43 years of age, complained of a dull, aching pain in the upper portion of his abdomen, of which he had been aware for 1 year. The pain had been constant and had been somewhat intensified after meals. Some epigastric tenderness had also been present.

Analysis of gastric contents revealed a total acidity of 70, free hydrochloric acid of 50, and a total quantity of 175 cubic centimeters. The roentgenologic diagnosis was prepyloric ulcer.

At exploration, a diverticulum, 4 centimeters in diameter, was found on the greater curvature and removed by resection of the pyloric third of the stomach. A posterior Pólya anastomosis was made. The pathological diagnosis was diverticulum.

CASE 4. A woman, aged 30 years, entered the clinic because of stomach trouble during the previous 4 years. She complained of pain in the epigastrium following a heavy meal, which had been relieved by emesis and massage of the abdomen and partially alleviated by taking soda. Slight epigastric tenderness was present.

Analysis of gastric contents revealed a total acidity of 40, free hydrochloric acid of 32, and a total quantity of 35 cubic centimeters. The roentgenologic diagnosis was duodenal ulcer with moderate retention.

Fig. 9. Diverticulum of cardia. Fluid level is evident.

A diverticulum producing obstruction, 2 centimeters from the pyloric ring on the gastric side, was discovered. Pylorectomy was performed. The diagnosis of diverticulum was confirmed pathologically.

CASE 5. A woman, 26 years of age, came to the clinic because of dysphagia and spasmodic substernal pain that had been present for 10 months. She also had had pain in the epigastrium from 1 to 2 hours after meals. There had been some regurgitation at times. Dilatation of the œsophagus had relieved the substernal pain, but had failed to affect the distress in the epigastrium.

Exploration revealed a diverticulum, 3 inches (7.5 centimeters) deep, at the lower margin of the stomach near the pylorus. The lesion was excised and the pathologist's report confirmed the diagnosis.

Eighteen years later the patient complained of symptoms referable only to cardiospasm.

CASE 6. A man, 51 years of age, entered the clinic because of weakness, anæmia, and tarry stools during the previous 9 months. Examination of the blood revealed that the concentration of hæmoglobin was 43 per cent, that erythrocytes numbered 3,120,000 and leucocytes 8,100 per cubic millimeter, and that the color index was 0.7 per cent. There was a total gastric acidity of 90, free hydrochloric acid of 72, and a gastric content of 80 cubic centimeters. The roentgenologic findings were suggestive of a benign lesion at the pyloric end of the stomach.

On exploration, two diverticula containing clotted blood were found on the posterior wall of the stomach near the greater curvature and about 3 inches (7.5 centimeters) from the pylorus. The lesions were excised by sleeve resection of stomach. Pathologist's report confirmed diagnosis.

Definite signs of a blood dyscrasia developed later.

CASE 7. A man, 50 years of age, complained of vague, gastric intestinal disturbance not characteristic of any definite disease. Roentgenologic diagnosis was carcinoma of the stomach. A tumor on the posterior wall, 2 inches (5.0 centimeters) away from the pylorus was removed. The pathologist reported that the lesion was a diverticulum, 3 centimeters long, with a fibrosarcoma starting in the submucosa. The patient died subsequently from extension of the malignancy.

CASE 8. A man, 49 years of age, was operated on because of gastro-intestinal symptoms indicative of peptic ulcer. A diverticulum was found contiguous to a perforating ulcer at the pylorus. Excision and a Finney type of pyloroplasty were performed. The surgical findings were confirmed pathologically. Six years later, gastro-enterostomy was performed for recurrence of symptoms.

CASE 9. A woman, 29 years of age, was operated on because of symptoms ascribed to peptic ulcer. A duodenal ulcer was found. Adenomyoma in a diverticulum with an opening 2 centimeters in diameter, also was present. The diverticulum was on the lower border of the stomach, just proximal to the pylorus. Excision of the diverticulum and gastro-enterostomy were performed. The pathologist's report was confirmatory. Three months later the patient wrote that she was cured.

CASE 10. A woman, 59 years of age, was operated on because of symptoms indicative of peptic ulcer. A duodenal ulcer and a diverticulum, 1 centimeter in diameter in the pyloric region, were excised. A Billroth I anastomosis was performed. The surgical diagnosis was confirmed pathologically. One year later the patient complained of stomach trouble.

POSTMORTEM

CASE 11. A woman, 56 years of age, died following surgical drainage of an appendiceal abscess. Necropsy revealed among other lesions a large diverticulum of the cardia and diverticula of the colon.

CASE 12. A man, aged 49 years, died of cardiovascular-renal-disease. Necropsy revealed among other lesions a diverticulum, 1 by 1.5 centimeters which was situated 4 centimeters from the cardia.

CASE 13. A woman, 44 years of age, died following hysterectomy for carcinoma of the uterus. Necropsy revealed among other lesions a diverticulum, 1 by 1.5 centimeters in diameter, situated 8 centimeters below the œsophagus. A duodenal diverticulum also was found.

CASE 14. A woman, 55 years of age, died of carcinoma of the œsophagus. Necropsy revealed a diverticulum of the cardia partially covered by epithelium of the œsophageal type.

SUMMARY AND CONCLUSIONS

An effort has been made to review in some detail a relatively large group of diverticula of the stomach seen at the Mayo Clinic.

Diverticula in the stomach are rare and, to our knowledge, only 141 cases have been mentioned or reported in detail to date, including our 33 cases, 19 of which were not proved.

In 10 (74 per cent) of the 14 proved cases which we report, there were no symptoms referable to diverticulum; in 4, symptoms which may have been related to diverticulum were present.

The cause of true diverticula of the stomach is not definitely known. The hypothesis that they are congenital is plausible. The cause of the acquired types usually is obvious.

The situation of gastric diverticula in cases reported in the literature was most often at the cardia and next most often at the pylorus, although they have occurred in every portion of the stomach. In our series the diverticula were equally distributed at the cardiac and pyloric regions of the stomach.

Associated peptic disease was present in 4 of our 14 cases (30 per cent) and consisted of gastric ulcer, duodenal ulcer, adenomyoma, and sarcoma. Similar associated lesions have been reported in cases in the literature.

The diagnosis is difficult. In our series 4 of 6 pouches diagnosed roentgenologically as diverticula proved to be pouches which developed as a result of perforating ulcers or malignant lesions.

Complication occurred in only 1 of our cases and, in that instance, consisted of hæmorrhage. Such hæmorrhages have been reported by other writers.

In view of the fact that it is extremely difficult to ascertain with accuracy the nature of a diverticulum of the stomach, it would seem to us that with roentgenologic evidence of such a condition and the presence of indigestion, it would be safer to advise surgical exploration.

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EDITORIALS

SURGERY, GYNECOLOGY AND OBSTETRICS

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JANUARY, 1935

IDIOPATHIC DILATATION OF THE SYSTEM OF EVACUATION

SURGEONS who perform operations on the sympathetic nerves to the viscera in the pelvis are becoming familiar with coexistent dilatation of the sigmoid colon and possibly rectum, the urinary bladder, and the ureters. As a rule the primary object of the operator has been to relieve the symptoms of Hirschsprung's disease by sympathectomy, and the dilatation of the lower urinary tract has not been suspected. Although there is still doubt as to the exact nature of the lesion that leads to the pathological changes in the colon characteristic of Hirschsprung's disease, the present consensus is that a congenital defect in the neuromuscular mechanism of the distal part of the colon is present. The proportion of cases of idiopathic dilatation of the colon that is associated with dilatation of the lower urinary tract is still unknown; but it is high enough to direct attention to the probability, and it is likely that the routine investigation by intravenous urography of patients suffering from Hirschsprung's disease will show the association to be common. In such cases the obstruction to the outflow of urine from the ureters and the bladder appears to result from achalasia at the ureterovesical junctures and at the internal sphincter of the bladder, respectively.

It is probably of significance that the dilated structures receive their sympathetic innervation from the same source—the superior hypogastric plexus or presacral nerve—and this view is supported by the degree of success that has attended efforts to overcome these neuromuscular obstructions by resection of the nerve. A single anatomical lesion cannot be responsible for all the cases that fall into this broad group, for indubitably the dilatation may be confined to the colon, to the ureters and bladder, to the bladder alone, or to one ureter. The pathology of the condition is even more obscure.

Of more practical moment to the surgeon is the early recognition, and if possible correction, of this state of affairs. The lesions involve the structures that are concerned in the final ridding of the body of its waste products—the system of evacuation—and inefficiency of this system must sooner or later prove fatal. Sympathectomy for Hirschsprung's disease appears to be a well-tried and satisfactory operation. One of the most important factors in determining its effect on the urinary tract appears to be the state of the walls of the ureters, for long continued stasis and infection of urine may lead to changes of a chronic inflammatory nature which destroy their contractility. But the whole matter is far from surgical finality.

J. R. LEARMONTH

THE SURGICAL TREATMENT OF HYPERTENSION

ONE of the latest developments in the field of surgery of the sympathetic nervous system is the treatment of hypertension. Secondary forms of hypertension, such as those associated with nephritis and arteriosclerosis, as well as the paroxysmal form associated with suprarenal tumors, are not included in the group to be considered for this type of surgery.

The type of hypertension that has responded to operations on the sympathetic nervous system is the primary or constitutional form which occurs among comparatively young people, is progressive in spite of medical treatment, and carries a prognosis comparable to that of malignant neoplasms. This severe type of essential hypertension may be designated as the malignant type. Because no definite etiological factors have been found, it has been assumed that a constitutional neurogenic abnormality plays an important part in the disease. Following this assumption, and because vasospastic diseases which are due to neurogenic imbalance have been relieved by sympathetic ganglionectomy, operations on the sympathetic nervous system have been carried out in an attempt to relieve hypertension.

There is close parallelism between the disturbed vasospastic mechanism of Raynaud's disease and that of primary hypertension. In both conditions hyperactivity of the vasomotor center in the brain is believed to be at fault. Since surgical interruption of the vasomotor fibers to the extremities relieves the symptoms of Raynaud's disease, it is rational to believe that interruption of the vasomotor nerves to a large portion of the vascular tree would have a depressor effect.

Among the first operations for relief of hypertension were sympathetic denervations of the upper and lower extremities. This did not affect a sufficient portion of the arterioles to modify the systemic blood pressure, and so, desiring to denervate not only the vessels of the lower extremities but also those of the abdominal cavity, the spinal roots from which sympathetic fibers proceed to the latter region were divided. In order to accomplish this, it seemed necessary to perform laminectomy and rhizotomy of the anterior and posterior roots from the sixth thoracic to the second lumbar segments, inclusive.

Following this operative procedure there was noted a definite and significant drop in blood pressure. In addition to interruption of the vasomotor fibers, there was paralysis of the abdominal muscles, which reduced the intra-abdominal pressure. While the desired effects on the blood pressure were achieved, the procedure was considered too radical as a routine form of treatment and a less hazardous procedure was sought. In view of the fact that the splanchnic nerves carrying the sympathetic fibers from the anterior roots to the abdominal viscera could be approached by a less extensive operation, they were resected as they entered the abdominal cavity between the crura of the diaphragm. Following this type of operation, a definite drop in blood pressure occurred and definite relief of symptoms was noted in milder and earlier cases, although results did not seem so satisfactory in the more advanced cases. For that reason the previously described rhizotomy was modified to the extent that only the anterior roots were divided. This procedure proved effective in bringing about a significant lowering of blood pressure.

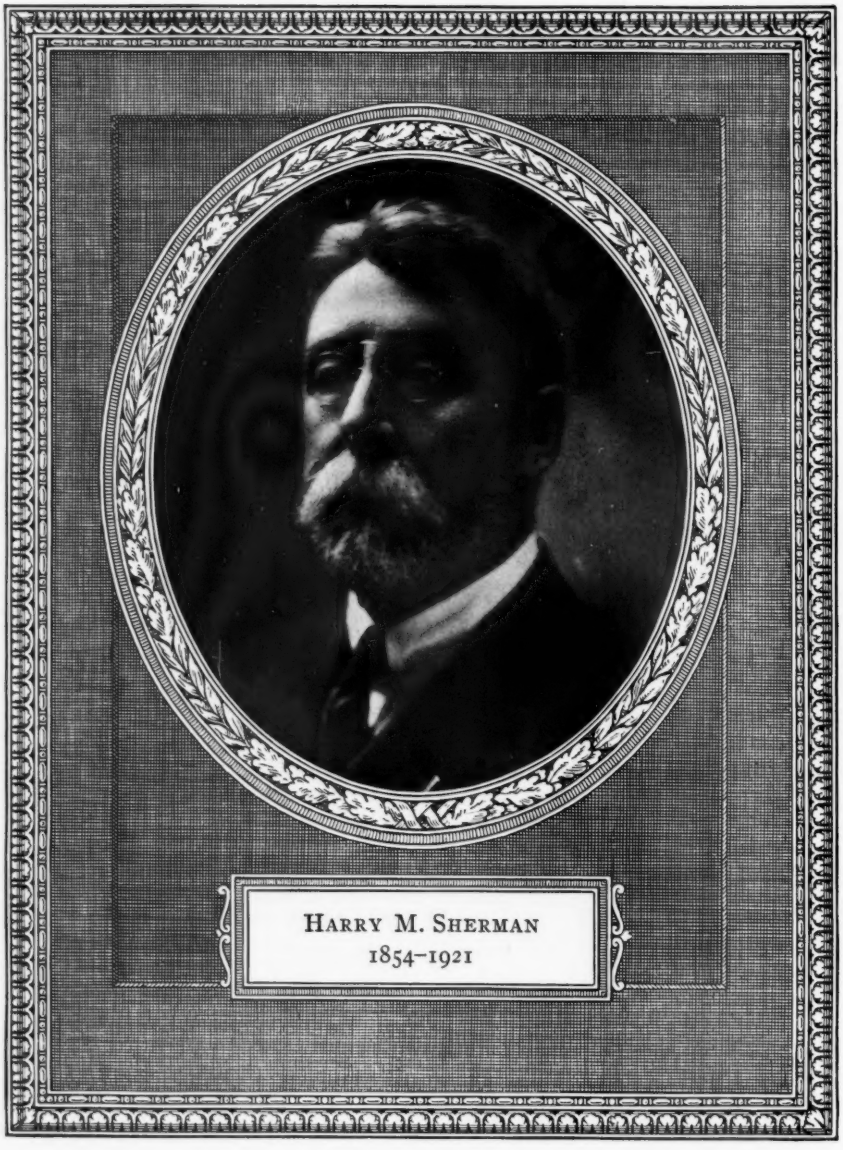
A further modification of this type of operative procedure consisted of the division of the ninth thoracic to the second lumbar roots, inclusive, in an effort thereby to produce a maximal drop in blood pressure with a minimal amount of risk.

Several important observations have been made following the two types of rhizotomy. There have been no noticeable deleterious effects, except possibly slowing of the excretion of water, which has not resulted in serious complication. Absence of sweating over the abdomen and lower extremities testifies to the division of the vasomotor fibers. There is a postural drop in blood pressure in that the pressure is higher when the patient is prone and lower when the patient is erect. Lessened response in blood pressure to psychic, thermal, and pain stimuli has been noticed, and marked change in the mean levels of both diastolic and systolic pressures has been maintained over a sufficient time to indicate definite therapeutic value.

It may seem radical to advise resection of the splanchnic nerves or extensive laminectomy and rhizotomy for patients who have this type of hypertension but who have very few symptoms, yet, in the light of experience, it would seem that if operation is to be done at all, it should be done before changes in cerebral, retinal, and renal arteries are too advanced.

In spite of the fact that cases are on record in which patients have been followed for two years after splanchnic resection and four years after rhizotomy and beneficial effects have persisted for these periods of time, this type of treatment of hypertension should be considered as investigative and more or less experimental until a larger series of patients have been treated and more time has elapsed for postoperative observation. If surgery of the sympathetic nervous system should prove of as permanent value in the control of progressive, primary, constitutional hypertension as it has in the treatment of some of the vascular diseases affecting the extremities and of other conditions in which hyperactivity of the sympathetic nervous system has been of etiological importance, then it will have achieved another victory in the treatment of a disease which has been found to be resistant to all other forms of therapy.

WINCHELL MCK. CRAIG.



HARRY M. SHERMAN
1854–1921

MASTER SURGEONS OF AMERICA

HARRY MITCHELL SHERMAN

HARRY MITCHELL SHERMAN, the first specialist in orthopedic surgery on the Pacific Coast, was born in Providence, Rhode Island, November 23, 1854. His paternal ancestor came from England in 1633. On his mother's side, the family were descendants of an old French Huguenot family, Mauran by name.

His preliminary education was in St. Paul's School, Concord, New Hampshire, and in 1877 he was graduated as Bachelor of Arts from Trinity College, Connecticut. His medical degree was from the College of Physicians and Surgeons, New York, in 1880, which college later became the Medical Department of Columbia University. In that same year, Trinity College granted him the degree of Master of Arts. His hospital interneship was in Bellevue, New York, and he served for a time as assistant surgeon at West Point Foundry, New York. In 1881, he became assistant to Dr. Murdock at Cold Spring-on-the-Hudson, and later had some experience as ship surgeon on one of the steamships of the Alexandre Line.

In February, 1885, he came to San Francisco and entered practice, soon becoming associated with the late Dr. George Chismore, the eminent urologist.

Since he had had special training in orthopedic surgery with Dr. Lewis A. Sayre in Bellevue, he recognized in San Francisco an opportunity to develop that specialty, which until then had been in the hands of general surgeons.

In 1886, he became orthopedic surgeon to the Children's Hospital, San Francisco, organized in 1875 by a group of women headed by Dr. Charlotte Blake Brown, and he soon made that institution the center of orthopedic surgery on the Pacific Coast.

In 1890, he married Matilda Barreda, daughter of Frederick Barreda, Peruvian minister to the United States. Mrs. Sherman died in 1895, leaving one son, Frederick Barreda Sherman. In 1896, Dr. Sherman spent a year in Vienna, studying orthopedics.

In 1900, Dr. Sherman married Lucia Hamilton Kittle, daughter of J. G. Kittle, of Ross, California. Of this marriage, there were two daughters, Lucia Kittle and Isabel, who, with the son, Frederick Barreda, and Mrs. Sherman, survive.

Dr. Sherman suffered from asthma for a number of years, but notwithstanding this handicap, he had an unusually full professional life, with great accomplishment. Finally his heart broke down after an attack of influenza, and he died May 15, 1921.

Dr. Sherman was made clinical professor of orthopedic surgery in the University of California in 1896, and professor of the principles and practice of surgery in 1899, which position he held until 1912. In 1901 he was appointed surgeon to St. Luke's Hospital, San Francisco, where he did much operative work. He recognized that in cleft palate work he could see in the depth much better if he had dark instead of white draping. He therefore experimented with colors in the operating room and finally hit upon dark green tiling and dark blue draperies and gowns as most restful to the eye, favoring illumination of the depth of surgical wounds. Like other of Dr. Sherman's original notions, the green color has been chosen for the tiling of operating rooms in numerous other institutions.

He was an active member in many surgical organizations—The American Orthopedic Association, 1899 (president in 1900), The American Surgical Association, 1905. In 1912, he was one of the organizers of the San Francisco Polyclinic and later did yeoman work in organizing the American College of Surgeons in California, of which organization he was one of the governors. It is of some interest to note that after the San Francisco earthquake and fire of 1906, Dr. Sherman was the inspiration for the opening of a teaching hospital for the University of California Medical Department—he started with one bed and one patient, he himself furnishing the equipment—an institution which has become one of the most prominent teaching hospitals in the country.

While Dr. Sherman's chief work was in orthopedics, he did not limit his efforts to that specialty, but did much creditable work in other fields—cleft palate, surgery of the spleen, surgery of tumors, and even brain surgery. He did much experimental work on suture of heart wounds. He operated a number of times for the removal of the gasserian ganglion for facial neuralgia, and it is fair to assume that the broader view of pathological problems thus acquired reacted to the betterment of his orthopedic surgery.

Endowed with tireless energy, he gave much time and thought to matters of public welfare. In his relations with his fellow man, he was always the gentleman in the best sense of the word.

In the late war, having been for some years an officer in the Medical Reserve Corps of the United States Army, he was called to active duty, with rank of major, and served as surgeon in command of the Army Hospital at Fort Rosecrans, San Diego, until the end of the War. As a teacher, and in his clinical work, he was painstaking to an extreme and his private and hospital records are models of concise, systematic work, largely in his own hand.

Of Dr. Sherman's contributions, perhaps the following are most noteworthy:

Open operation for congenital dislocation of the hip, in which he overcame the usual rotation of the femur by an infratrochanteric osteotomy, holding the fragments in proper position by means of drills or spikes incorporated in the plaster-of-paris dressing. A more fundamental idea was the use of sterile salt solution as a filling for cavities in bones and other places, Sherman making the point that the fluid was eventually replaced by blood into which bone gradually grew, and the irritation from foreign bodies such as the various pastes which had been previously used, was avoided.

He invented an extremely useful instrument, a spreader for opening plaster-of-paris splints.

In 1902 he presented a notable paper before the American Surgical Association on the surgery of the heart.

Dr. Sherman's position as surgeon is not to be measured by his contributions to literature, for they were not numerous, though of telling quality, but by his influence on those who came into contact with him, for they could not fail to catch some of his enthusiasm. He was a careful and thorough clinician, an excellent operator, a splendid teacher, who had the faculty of attracting young men to his work, and it is noteworthy that the present generation of orthopedic surgeons in San Francisco were nearly all Sherman's students.

EMMET RIXFORD.

EARLY AMERICAN MEDICAL SCHOOLS

THE HISTORY OF RUSH MEDICAL COLLEGE

GOLDER LEWIS McWHORTER, M.D., PH.D., CHICAGO

RUSH MEDICAL COLLEGE was granted a charter on March 2, 1837, antedating that of the city of Chicago by several days. It was the only medical school in Chicago until 1859 and the only one of five pioneer medical schools in that vicinity to continue without interruption to the present time.

Largely to Daniel Brainard (Fig.1) must be given the credit for its establishment and early development. Arriving in Chicago in 1836, only two years after his graduation from Jefferson Medical College, he soon demonstrated unusual foresight, ambition, and executive ability. Chicago, at this time, was a rapidly growing village of three thousand. In the adjacent community were many practitioners who had received either no medical education or had failed to graduate, while only about 20 per cent of them were medical graduates. Due to the poor transportation, the demand for physicians was great and the expense together with the inaccessibility of the few eastern medical schools placed the study of medicine largely beyond the reach of possible students from the local community.

Resulting from the local need at this time, there developed five pioneer medical schools in the vicinity of Chicago.

The medical department of LaPorte University was founded in 1842. It became the medical department of Indiana Medical College in 1848 and was discontinued in 1850.

Franklin Medical College was organized at St. Charles, Illinois, in 1842 and discontinued in 1849.

The medical department of Illinois College at Jacksonville was established in 1843 and discontinued in 1848.

Rock Island Medical School was organized in 1848, moved to Davenport, then to Keokuk, and later became a part of the University of Iowa.

Rush Medical College was named after Dr. Benjamin Rush (1745–1813) of Philadelphia. He was one of the foremost medical men and citizens of his time, a graduate of Princeton in 1760, Edinburgh in 1768, professor of medicine in the University of Pennsylvania, a signer of the Declaration of Independence, and treasurer of the United States mint from 1799 to 1813.

In his publications in 1854, Daniel Brainard did not appear to favor the name Rush. He termed himself professor of surgery of the Medical College of Illinois at Chicago and later called it the Medical College of Chicago without mentioning the name Rush. Perhaps the lack of more than grateful appreciation by the relatives of Rush, to the commemoration of his name, at a time when the College was in serious financial straits was the reason.

Although a charter was obtained in 1837 with the expectation of an early opening of the school, economic conditions were very bad and it would probably not have opened in 1843 but for the organizing of the schools at LaPorte and St. Charles. This forced Daniel Brainard to open Rush sooner than he wished.

As a result an announcement was issued in October, 1843, stating that the first session would begin December 4, 1843, and continue for 16 weeks, before obtaining a college building. The lectures were given in the second story of a frame building occupied by Dr. Brainard as his office and next door to his home, at 49 South Clark Street, at the south east corner of the alley south of Lake Street. The requirements for the degree of doctor of medicine were, "Three years study with a respectable physician, two courses of lectures, one of which must be in this institution (or two years practice will be received in lieu of one course). The candidate must be 21 years old; of good moral character; must present a thesis on some medical subject of his own composition, and in his own handwriting, which shall be approved by the faculty; and pass a satisfactory examination on all the branches taught in this College."

The first course was given to a class of 22 students with one graduate. The instruction was given by four men with an average of four lectures a day. From the first, clinical teaching was established in the dispensary. This was opened by Dr. Blaney in 1839 as the first free dispensary in Chicago. Upon the opening of the College

in this block in 1843, it was transferred to the College quarters. In 1845 this dispensary was moved to Wolcott and Kinzie Streets and called the City Dispensary. Later it was adopted as a county institution.

During the summer of 1844 a building for the College was erected north of the river at Indiana and Dearborn Streets at a cost of about $3500.00 (Fig. 2). This served without a change for eleven years. The land was donated by interested real estate men while the faculty and a few others furnished the money.

Austin Flint, as professor of medicine, gave the introductory address in the new building, the first annual anniversary of Rush. He remained only one year, due, partly to an inadequate income from the ticket fees by the students.

Medical instruction at first given by a few of the leading physicians in the larger communities was now rapidly taken over by these pioneer medical schools. With the phenomenal growth of Chicago and the strong faculty at Rush it soon became the dominant medical school. There was also considerable feeling against them in the smaller communities because of the necessity for grave robbing, and many gruesome tales are told of these early teachers of anatomy and their students who had to obtain their own specimens for dissection. The robbing of a grave at St. Charles caused local indignation to run high with the death of one student and the closing of that medical school in 1849. It was not until 1885 that the State of Illinois legalized the disposition of unclaimed bodies to medical institutions for use in teaching.

By 1850 three of the other five pioneer medical schools had discontinued and a fourth had moved west of the Mississippi River. Five hundred and thirty-two students had studied and 132 had graduated from Rush which had now become strongly established.

While these pioneer medical schools were often referred to as "proprietary" this was not literally the fact, although the property rights did rest with boards of trustees which included medical men.

Among the original seventeen trustees of Rush, only one was a physician and he was not on the faculty. However, shares of stock in Rush Medical College were issued and sold largely to the faculty members who, from time to time, were called upon to finance the institution. Dividends were also paid upon this stock.

In the summer of 1850 Chicago had a population of over 25,000. The United States Marine Hospital located only a short distance from the

Fig. 1. Daniel Brainard, 1812–1866.

College was nearing completion. Professor Herrick of the College assumed charge and clinics were held there in 1853–54.

The Illinois General Hospital of the Lakes, or the "Lake House" was organized with a lying-in department. It came under the management of the Sisters of Mercy and after the first year was called Mercy Hospital. In 1851–52 Professors Brainard and Davis were in charge of the surgical and medical services and held clinics there. In the College announcement of that year there appeared, but not without some objection, the notice that the requirements of graduation would include hospital attendance.

In 1855 the College building was enlarged to accommodate about 250 students at a cost of $15,000.00 sustained by the faculty. A museum was included with space for many specimens which had been collected by Professor Brainard in Europe.

In 1856 the College announcement contained a defence of hospital ward teaching as practiced the preceding four years in the Mercy and Marine Hospitals.

Early in 1859 N. S. Davis and a group of the faculty who favored a graded course of instruction resigned and founded what was for a time known as the Medical Department of Lind University, afterward as the Chicago Medical College, and later the Medical Department of Northwestern University, Mercy Hospital being used for their clinical teaching.

Fig. 2. Rush Medical College building erected in 1844.

Rush Medical College then announced that in addition to the Marine Hospital, they would use the newly opened 200 bed City Hospital for teaching. Following the Civil War the City Hospital was taken over as the Cook County Hospital in 1866.

A course of lectures was inaugurated in the spring and early summer in 1859 by the Rush faculty. In 1860 the College announcement called it the Chicago Summer School of Medicine. This was later called the spring and summer lecture course of Rush Medical College and continued almost without interruption until the regular course was extended to 8 months in 1893. In 1860 the College announced a preliminary course of lectures of 2 weeks in addition to the regular course of 16 weeks.

Daniel Brainard died of Asiatic cholera October 10, 1866, aged 54 years, during an epidemic in Chicago, then a city of 200,000. Despite this the College continued without interruption.

In May, 1867, the corner stone of an additional building containing an amphitheater with 625 numbered seats was laid and the old structure remodeled at a cost of about $70,000.00 which was financed by the faculty.

In the spring of 1867, Moses Gunn was invited to the chair of surgery and for 20 years until his death rendered a great service to the institution. In 1867 the requirement of a formal thesis was abandoned and the regular course was increased from 16 to 18 weeks. In 1871, it was increased to 20 weeks.

On October 9, 1871, during the great fire the buildings of the College were burned. There was almost a complete loss from the fire and Rush was left $65,000 in debt largely to the faculty.

Teaching was continued in a clinical amphitheater of the Cook County Hospital and in the dissecting rooms of the Chicago Medical College generously offered to them. The rebuilding was delayed until the permanent location of the new County Hospital could be determined so that the College building could be erected adjacent to it.

During this period a temporary crude brick structure for lecture and dissecting rooms, costing about $4000.00 was built on the grounds of the old County Hospital at 18th and Arnold Streets. The College occupied this for 4 years from 1872 to 1876. The corner stone of the building at the present location, the corner of Harrison and Wood Streets, chosen because it was diagonally opposite the new Cook County Hospital was laid November 20, 1875. The formal opening took place on October 4, 1876 (Fig. 3). The lot and building cost about $54,000.00. Most of the money was obtained from the faculty and $11,000.00 from the Central Free Dispensary which occupied the first floor.

From the first use of the Blaney Dispensary Rush has always maintained the importance of clinical teaching. When the first building was erected clinics were held there for the medical and surgical treatment of patients before the students. This dispensary was abandoned with the burning of the building in 1871. The County Hospital

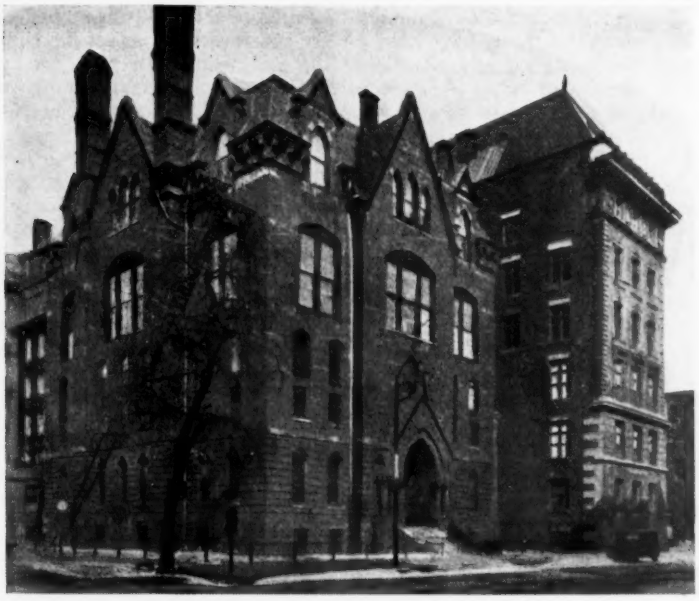


Fig. 3. The corner building of Rush Medical College which was used from 1876 to 1924, when it was replaced by the Rawson Building. Senn Hall in the background is still in use.

clinics were used until the opening of the new building in 1876.

The Central Free Dispensary was organized May 4, 1867, under the title of the Brainard Free Dispensary and was supported at first by private donations, occupying small rooms at 239 W. Randolph Street. In 1873 it was united with the Herrick Free Dispensary, founded in 1871. The endowment at that time was brought up to $11,000.00, which in 1875 was lent to Rush for a first mortgage on the lot. The College agreed to provide rooms for the dispensary and to furnish medical service with the privilege of using the patients as teaching material for the students.

While these quarters were changed in June, 1902, to Senn Hall and later back to the Rawson Building the clinical teaching in the dispensary has never been interrupted. The dispensary and the affiliation with the Presbyterian and Cook County Hospitals may be called the three principal assets of Rush Medical College. The Presbyterian Hospital was organized and building started in 1883 through the efforts of the faculty and an agreement made so that it could be used for teaching purposes. The staff of the hospital almost without exception has always been composed of members of the faculty of the College.

In 1882 for the first time a preliminary examination required in English, physics, and mathematics was held for those matriculating in Rush unless they were graduates of accredited high schools or their equivalent. This was necessary to qualify for practice in Illinois (1884). At this time instruction in the College began to assume a graded character.

In 1877 the regular course was increased from 20 to 21 weeks.

In 1879 the College urged, but did not require for graduation, attendance at the spring and summer terms, in addition to the regular term of at least 2, if not 3 years, with a minimum of 3 years of study as heretofore. The period of study was divided into six terms over 3 years.

In 1887 the College required, in addition to studying medicine at least 3 years, that the minimum of two required courses of lectures for the degree of medicine must not have been delivered in "one twelve-month.'

After the death of Moses Gunn in 1887, Charles T. Parkes was given the chair of surgery and Arthur Dean Bevan, a graduate of Rush (1883), was elected to the chair of anatomy. In 1888 Nicholas Senn was given the chair of principles of surgery and surgical pathology.

In 1889 the College announced that beginning in 1891 three full courses of lectures, at least 6 months each, would be demanded for graduation.

In 1891, at the death of Charles T. Parkes, Nicholas Senn was given the chair of surgery.

In 1892 the announcement stated that each matriculate, in accordance with the state law, must study medicine 4 years and take three courses of lectures of at least 5 months each. The College requirements for graduation were increased to 4 years of study and an attendance at three courses of lectures of 6 months each.

In 1893 the regular course was made to cover 8 months and the spring course was discontinued.

A new laboratory building was dedicated on December 4, 1893, just 50 years after the beginning of the first course of lectures.

In 1894 it was announced that after 1895 four full courses of lectures would be required of 8 months each in graded courses. This requirement was changed to go into effect June 1, 1897. At this time (1897), the College still held preliminary examinations for students who were not graduates of high schools or their equivalent.

The early affiliations of Rush Medical College are only of historical interest, as they created no change in the methods of teaching or indeed affected the College in any noticeable manner.

In the annual announcement for 1862–63 Rush Medical College was recognized as the medical department of the University of Saint Mary's of the Lake, located at the corner of State and Huron Streets. No further notice was ever made.

On May 1, 1875, plans were made for Rush to become a department of the old University of Chicago. Although so described in the announcement of 1874–75 the union was never consummated and the subject was never mentioned again in the meetings of the trustees of the College.

In June, 1887, Rush Medical College became the Medical Department of Lake Forest University, but it did not involve any close relations and each retained its own autonomy. This relation was dissolved by mutual consent in April, 1898, and almost immediately the affiliation of the College with the University of Chicago was established. The affiliation of Rush Medical College in June, 1898, marked an epoch in medical education not only in the College but in the history of medicine in America.

By the terms of this affiliation, the College surrendered control of its property to the University, which at this time made it clear that it was not its intention for Rush to necessarily become its medical school. The University stated that it proposed to establish its own medical school when funds became available. Rush adopted as far as possible the general regulations of the University. One of the most satisfactory has been the continuous session, or four quarter arrangement, of the college year. This was established for the session of 1899–1900, when the first 2 years of the medical course was transferred to the University.

The increased requirements led to a falling off of the number of students, the lowest being in 1905–06 when the freshman class numbered about 65. This was a marked contrast to the classes of 200 to 250 which was the rule in the preceding years. Few changes were made in the clinical faculty except to increase it somewhat in numbers.

Since 1914 the requirements have included a fifth year consisting of a hospital interneship or of a fellowship in one of the departments.

With the death of Nicholas Senn in 1908, Professor Arthur Dean Bevan succeeded him as head of the department of surgery. In 1934 Dr. Vernon C. David was given the chair of surgery at the retirement of Professor Bevan who had served his Alma Mater as a teacher for 46 years.

In May, 1924, a new contract was executed between the Corporation of Rush Medical College and the University of Chicago, in accordance with which the affiliation of 1898 was superseded and the University took over the work of the College as a department. This went into effect June 16, 1924. Thereafter only the last two years of clinical work has been offered by Rush Medical College.

With the organization of the School of Medicine of the Division of the Biological Sciences of the University of Chicago, the work of the first 2 years of medicine, formerly given in co-operation with Rush, was increased to include the third and fourth clinical years, in the university hospitals and clinics. It was so arranged that the work of the third and fourth years could be taken either on the quadrangles or in Rush Medical College. In 1924 the old college building, used since 1876, was replaced by the Rawson Clinical Laboratory and the Norman Bridge Laboratory of Pathology.

Before the affiliation of Rush with the University there were 5,225 graduates. To September, 1934, there has been a total of 9,917 graduated from Rush Medical College.

Rush Medical College, through the efforts of its faculty, by means of its opportune and successful affiliations with clinics, hospitals, and the University of Chicago, and through the discoveries and services of the physicians who have studied there, has achieved immortality. May Rush so continue, as in the past, to signify the best in medicine.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE fourth edition of Blair-Bell's most excellent textbook of gynecology[1] has been expanded and enlarged in its scope. Chapters have been added on the history of gynecology, on ethics, and on the medicolegal aspects of gynecology. It is gratifying to find a chapter on contraception even though the discussion of this subject leaves much to be desired. The author might well have made this chapter more complete, since reliable information on this subject has not yet found its way into the standard textbooks.

The chapters on the problems in endocrinology, on endometriomata, and on malignancy have been rewritten and brought up to date. Many new illustrations have been added throughout the book. The admirable style in which the previous editions have been written, has been carried over into this edition. This work should continue to be one of the standard English textbooks of gynecology.

RALPH A. REIS.

THE fascinating story[2] by Frederick Watson of the life of Sir Robert Jones, once begun, is difficult to lay down until one has read to the end. "The story tells itself" so simply and directly that the reader hardly realizes until he has completed it that this book is beautifully written and a very great credit to the writer's art.

If one could sum up the story of Sir Robert Jones' life in a few words they would be that he was a man loved far above the measure which usually falls to the lot of men. Throughout his life and work that devoted affection of family, associates, friends, patients, and even casual acquaintances, stood out predominantly, and furnished the most potent factor in the influence he wielded and the results he was able to achieve in behalf of the causes which moved him so strongly.

Fortunate in his parental background and early home life, he was equally fortunate in the opportunity that came to him at the age of 16 to enter the home of his aunt Elizabeth and her husband, Hugh Owen Thomas. In Watson's words:

> To live under the same roof with Thomas must have been a daily adventure. His passion for work and his asceticism of life did not remove him from his wife and her young nephew. There were always the evenings or part of them. At the end of a long day's toil he would work on his lathe, or play the flute, or discuss in his uncompromising fashion some aspect of life or literature. His range of knowledge upon the most academic subjects was remarkable, and his attitude toward all topics strongly coloured by rationalism.

During these years of Jones' apprenticeship Thomas had an immense practice, and Jones literally grew into the practice of orthopedic surgery and under unusually fortunate conditions.

> Between 1870 and 1900, Nelson Street [where Thomas lived] was responsible for the medical supervision of the shipwrights, ironworkers, boilermakers and dockgate men of Merseyside. The accidents from such employments were continuous and severe. Those were still the days of sailing ships, as well as steam, and the old case-books show a steady procession year in and year out of ship's captains, carpenters and seamen of all grades and nations, who had suffered injury at sea or in port. These cases came straight to Nelson Street and were treated there from start to finish, to the advantage alike of patient and surgeon; for whereas the former received what was practically specialist attention, the surgeon's gain was the observation of injuries of every kind and at every stage. Thomas never held a hospital appointment. But he was not a loser by that, for although he remained to the end of his life outside the professional camp, he alone was able to treat his cases from start to finish in his surgery and nursing homes.

and

> It was to relieve the terrible distress of these people [of the slums] that Thomas opened his free Sunday clinic, where, assisted by a large staff, he laboured from early morning throughout the day. It was at these Sundays that the spectacle of deformed babies and young children first set the mind of Robert Jones upon the problem of crippling diseases.

In 1891 Thomas died, and shortly after Jones moved again from 22, Great George Square, where he had established himself in 1885, to 11, Nelson Street. From that date until 1914 the story is one of almost uninterrupted and joyful work at 11, Nelson Street, at the Royal Southern Hospital, and at Baschurch, the open air hospital for crippled children founded by Miss Agnes Hunt.

A distinguished American surgeon has written of this period:

> Mr. Jones begins his day after an early breakfast at 7:30 by visiting his patients at their homes or in his private hospitals where they have been placed. About 11 o'clock he returns to his office, where he passes quickly from one patient to another in the various rooms, spending but a moment with each, but seizing at once with an almost intuitive instinct upon the nature of the affection and the essential indication for treatment. Small operations, such as tenotomies and mobilization of adherent joints, are often done on the spot, his lively optimism and cheerful tact being in many cases the only anæsthetic employed. A dozen cases are started, none are finished, patients crowd the rooms and wait in corridors, everything to the outsider is hopeless confusion, but one thread after another is picked up by the busy master, one difficulty after another solved on the spot, order is brought out of chaos, and in an incredibly short space of time each patient had had the proper diagnosis and the proper treatment applied.

[1] THE PRINCIPLES OF GYNÆCOLOGY; A TEXT-BOOK FOR STUDENTS AND PRACTITIONERS. By William Blair-Bell, B.S., M.D. (Lond.), F.R.C.S. (Eng.), F.C.O.G. (Hon.), F.A.C.S. (Hon.), LL.D. (Glasg.). 4th ed. rev. with the assistance of M. M. Datnow, M.D. B.Ch. (Liverp.), F.R.C.S. (Edin.), M.C.O.G., and Arthur C. H. Bell, M.D., B.S. (Lond.), F.R.C.S. (Eng.), M.C.O.G. Baltimore: William Wood & Co., 1934.

[2] THE LIFE OF SIR ROBERT JONES. By Frederick Watson. Baltimore: William Wood & Co., 1934.

and has been instructed about home management and when to call again.

The writer has never seen anything approaching this mastery of the clinical material or of the technical means. This was equally displayed in the work at the Royal Southern Hospital, where Mr. Jones has a surgical service. On his regular operating day, Wednesday, he often exceeds twenty operations. On the Wednesday at which the writer was present he did twenty-six; beginning at 2:30 p.m., he finished at 9:00, doing every operation himself but one, which was done by the house surgeon. The operations were done on a table, which was also used as a stretcher, and by having two of these stretcher-tables and two anæsthetists, the operations followed each other with almost clocklike punctuality, at an average interval of fifteen minutes, and without any appearances of haste. When one considers that this included dressing in most cases, and that there were three knee resections, and other operations of equal importance, the performance seems little short of marvellous. All the operations but one were undertaken for the relief of deformity or joint disease.

Here, as in the office practice, the striking thing was the clear and quick appreciation of the gist of the matter in hand, and the instant application of the simple and effective remedy. Another striking feature of the work was the hearty and intelligent cooperation of his associates. Mr. Jones has attracted to himself a group of young men of skill and experience, who vie with each other in their devotion to him and to the work, and whose team play, if I may use the expression, is remarkably effective; there is no question by precedence, the right man is always on hand to do the right thing in the right way. The spirit of the place is as fine as the work and personality of the master.

With the trying days of 1914 came Sir Robert Jones' great opportunity, but opportunity freighted with grief and great responsibility. How well he acquitted himself, and how ably he discharged that responsibility cannot be told in a few words. Most American surgeons are familiar with the story, and both the older surgeons and those who 20 years ago were too young to appreciate its significance will delight in reading it in Watson's book. It has added still greater luster to that of the profession in which we are proud to be enrolled. It has been beautifully summarized by an anonymous writer in the *Journal of Bone and Joint Surgery* (vol. 15, page 542):

Behind his genial, smiling countenance, and apparent simplicity, Robert Jones possessed the keenest brain, the most brilliant organizing ability, and the tact, the patience, the perseverance and the astuteness of a diplomat. Never was man faced with greater difficulty or with more serious opposition than he was in the early days of the War, when he was entrusted with the establishment of the first military orthopædic service of this or any other country. He was appointed to the war office as Director of Orthopædics with the rank of Hon. Major General. England's home service began with 200 beds at Alder Hey in Liverpool; but within a short time the help of many English and American Surgeons was enlisted, and 33,000 beds were equipped and staffed with trained orthopædic surgeons. The brain which had already solved the problems of the cripple in civil life readily adapted itself to the problems of war. Incredible as it may be, the gigantic task was accomplished and a complete service established from first aid treatment in the field to the last stages of re-education and after-care. In 1918 he continued and completed his military orthopædic work through his appointment as Hon. Consultant to the Ministry of Pensions. In recognition of his war services, His Majesty conferred upon him the C.B. and later a knighthood, and the United States Army awarded him the Distinguished Service Medal.

After the weary years of war were ended and its tragic aftermath had to some extent been cleared away Sir Robert Jones might well have retired to a life of ease and contemplation of years well spent. He had made "the main principles of Hugh Owen Thomas acceptable to the medical profession," and had established the specialty of orthopædic surgery on a firm foundation. Instead of giving up, however, he plunged into the work that always seemed to crowd upon him more vigorously than ever. The cause of the cripple, which had always been so close to his heart, claimed a large share of his attention. To the organization of a national scheme for caring for the physically handicapped and for the prevention of tuberculosis and of rickets—those diseases which contributed so many new recruits to the army of cripples—he devoted that same energy and organizing ability which had accomplished so much for the wounded soldier. The map of England and Wales, dotted with strategically located orthopædic hospital schools and orthopædic clinics, tells better than words how successful his efforts were.

While continuing on a larger scale than ever the surgical practice which he had been forced to give up during the war he still found time to edit the *Orthopaedic Surgery of Injuries* which appeared in 1921, and to write in collaboration with Robert Lovett the *Textbook of Orthopædic Surgery* (1923) which "records for mankind" the principles and teachings which he constantly exemplified in his surgical work.

It seems incredible that in spite of advancing years he could still continue work and play at the strenuous pace that he set for himself, but

retirement, a leisurely old age, an opportunity to take things easily—all these would have been terrible to him. With ebbing strength, he surveyed the past and set no value on the future. If he could not be in the heart of the battle of life, he shrank from a place in the shadows.

In December, 1932, after a year of gradually declining strength he began to fail rather rapidly and on January 14, 1933 he "fell quietly asleep."

To have lived a life so fruitful, so filled with service to his fellow men, and to have gone to his last resting place loved and mourned by family, by associates, by students, by patients—in short by all who knew him—falls only to the lot of a fortunate few. Watson might well have added to his book the beautiful tribute which appeared in the *Journal of Bone and Joint Surgery* (vol. 15, pages 541–543) which begins and closes with the paragraphs:

The kindly word, the cheering smile, the twinkling eye, the whole magnetic personality of Sir Robert Jones remain only as a memory. The world's greatest orthopædic surgeon has completed his life's work; quietly as he was born seventy-four years ago at Rhyl on the North Wales coast, just as quietly he died in the early days of this year at a little village in Montgomeryshire.

and

Throughout his career he practised in Liverpool, and Liverpool has paid its last and greatest tribute to the honor of one of its citizens. The ashes of Sir Robert Jones are the first to find a resting place within the walls of the Cathedral. The urn stands on a column of stone, close to the foundation pillar, beneath the stained glass window dedicated to "Service." As long as the walls of that vast cathedral stand, they will shelter all that has died of Robert Jones, as a token and a memorial of his service to mankind. In the hearts and minds of those who came within the glow of his presenc and who learned humbly to love him, his spirit still lives.

SUMNER L. KOCH.

VOLUMES viii and ix of the twelve volume *Cyclopedia of Medicine*[1] edited by George M. Piersol and Edward L. Bortz are now available. (Review of first seven volumes appeared in the December, 1933, issue, page 822.) Volume viii continues the alphabetical arrangement of the subjects beginning with the letter "L" and the first topic is "Larynx, Disorders of." This section covers 69 pages and includes infections and nervous disorders together with the tumors of the organs. The section on metabolism is given 151 pages and covers proteins, fats, carbohydrates, and minerals. Myrrh is the last subject appearing in this volume and its pharmacology, preparations, dosage, and therapeutics are discussed briefly. Volume ix begins with the nails and a discussion of their structure, deformities, care, and disorders. A section of 70 pages is given to plastic surgery where technique is described and illustrated quite freely. The subject of pneumonia is well done. A discussion of potassium and its preparation and doses ends this volume. Attention is called to these topics only in that they indicate the general nature of the subject matter treated.

The volumes are 7 by 10 inches and the binding has been changed from the flexible to the conventional stiff type. The material is well arranged and the treatment of the subjects are concise and remarkably complete. M. HERBERT BARKER.

THE purpose of Dr. Vaughn's monograph[2] of 248 pages is to review the present position of the knowledge of the anæmias. She has been assisted by Professor H. M. Turnbull in the description of the pathological anatomy of various anæmias. In the first chapter, a review of normal erythrocyte measurements and a brief account of the anatomy and physiology of erythropoiesis are presented. The anæmias are classified under the general headings of dyshæmopoietic, post-hæmorrhagic, hæmolytic, and unclassified anæmias. The anæmias of infants and children are included in the classification and in the clinical descriptions. Each individual type of anæmia is considered from the standpoint of etiology, symptomatology, diagnosis, and treatment. Abundant reference to the literature is made throughout the text.

Under the grouping of the deficiency dyshæmopoietic anæmias, the recent conceptions and literature concerning iron deficiency anæmia and anæmia due to deficiency of the pernicious anæmia factor are presented. The relationship of this group to abnormalities of the gastro-intestinal tract is brought out. Under unexplained dyshæmopoietic anæmias, the author includes the less common leuco-erythroblastic anæmias. This type of anæmia was observed in diseases involving the bones which included carcinomatosis, myelomatosis, osteosclerosis, and Cooley's anæmia. It is suggested that these conditions do not cause anæmia by crowding out erythropoietic tissue but rather by depriving the blood cells of food factors necessary for normal ripening. Further under dyshæmopoietic anæmia, a description is given of erythroblastosis fetalis which includes hydrops fetalis, icterous gravis neonatorum and congenital anæmia of the newborn.

Dr. Vaughn has drawn frequently from her own experience in giving specific details of the findings in various anæmias. Characteristic diameters of the erythrocytes are illustrated in the accompanying Price-Jones curves. The material in general is presented on the basis of the evidence at hand and there is little if any tendency toward dogmatism. It is of interest that more than half of the articles from the large bibliography appeared after 1929. If hæmatologic research continues to progress as it has in the past, it is likely that this book will need revision in the near future.

This excellent monograph should be invaluable to the physician or student who wishes to familiarize himself with the revolutionary advances in the knowledge of the anæmias that have occurred in the past ten years. It should also serve as a valuable reference book to workers in the field of hæmatology.

HOWARD L. ALT.

IT is a pleasure to see Wright's *Applied Physiology*,[3] of which the first edition is dated 1926, already appearing in its fifth edition. Its remarkable popularity among medical students is due to a number of virtues too often lacking in the medical literature of the past. One of these is utmost conciseness of expression; it would be hard to find, in these 604 pages, a single superfluous word. Another is utmost concreteness of expression; for every generalization there is a specific instance, stated quantitatively when possible. These features adapt the book exactly to its purpose, which is to give an up-to-date summary of those facts of human physiology which have clinical application. It is not a book for a beginner, since introductory, historical, and laboratory-technical material is excluded. It is a book for the mature medical student who finds the clinical viewpoint stimulating in his study of physiology. It should also be helpful and interesting to physicians and surgeons who find that even conscientious reading of their journals sometimes fails to give a coherent idea of the present state of the science. Among the subjects which many readers will be particularly glad to have presented in this way, and to which special attention has been given in the new edition, are: blood groups, nephrosis, œdema, the anæmias, tissue oxidation, the carotid sinus, ischæmic pain, sympathectomy, cholecystokinin, the prolans, parathormone, and the hypothalamus.

FREDERIC T. JUNG.

[1] THE CYCLOPEDIA OF MEDICINE. George Morris Piersol, B.S., M.D., Editor-in-Chief, and Edward L. Bortz, A.B., M.D., Assistant Editor. Vols. viii and ix. Philadelphia: F. A. Davis Co., 1934.

[2] THE ANÆMIAS. By Janet M. Vaughn, D.M. (Oxon.), M.R.C.P. (Lond.). London: Oxford University Press, 1934.

[3] APPLIED PHYSIOLOGY. By Samson Wright, M.D., F.R.C.P. 5th ed. New York and London: Oxford University Press, 1934.

CORRESPONDENCE

CONCERNING A REGISTRY OF BRAIN TUMORS

To the Editor: A series of some two thousand tumors of the central nervous system collected by Dr. Harvey Cushing during his period of service at the Johns Hopkins Hospital and the Peter Bent Brigham Hospital has been brought to the Yale School of Medicine and put under the curatorship of the undersigned. It is intended that these elaborately catalogued specimens should so far as possible be made useful to those interested in the subject, and it is hoped that the collection will be added to from many sources.

There are many problems relating to tumor classification and expectancy of life after tumor removal that are as yet unsolved. Hence this series of cases may be of help to those who will encounter rare tumors that they wish to have identified if possible, and concerning which they may desire information, particularly on the basis of type prognosis.

Anyone who may feel inclined to send specimens for diagnosis or may seek information of other sorts is welcome to do so. The following persons, several of them already familiar with much of the material, have kindly consented to act as an advisory board:

PERCIVAL BAILEY, University of Chicago
F. C. GRANT, University of Pennsylvania
S. C. HARVEY, Yale University
G. J. HEUER, Cornell University
WILDER PENFIELD, McGill University
ERNEST SACHS, Washington University
W. P. VAN WAGENEN, University of Rochester
S. B. WOLBACH, Harvard University

LOUISE EISENHARDT, M.D., New Haven Hospital.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

THE TREATMENT OF INJURIES OF THE HEAD AND SPINE. By Jewett V. Reed, M.D. Indianapolis: C. E. Pauley & Co., Inc., 1934.

THE WELLCOME RESEARCH INSTITUTION AND THE AFFILIATED RESEARCH LABORATORIES AND MUSEUMS. Founded by Sir Henry Wellcome, LL.D., D.Sc., F.R.S. London, England: The Wellcome Foundation Ltd., 1934.

INTRODUCTION TO DISCUSSION ON GEOGRAPHICAL DISTRIBUTION OF CANCER IN SPAIN. THE CANCER OF 1932. By Frederick L. Hoffman, LL.D. Madrid: Blass, S. A., 1933.

TUBERCULOSIS OF THE LYMPHATIC SYSTEM. By Richard H. Miller, M.D., F.A.C.S. New York: The Macmillan Co., 1934.

COLLANDA DI MONOGRAFIE CHIRURGICHE. Directed by Prof. Raffaele Paolucci. VISCERITI E PERIVISCERITI; DIGESTIVE ADDOMINALI CRONICHE. By Francesco Zagarese. With a preface by Prof. Raffaele Paolucci. Bologna: Nicola Zanichelli Editore, 1934.

AN INTRODUCTION TO GYNECOLOGY. By C. Jeff Miller, M.D. 2d ed. St. Louis: The C. V. Mosby Co., 1934.

SYNOPSIS OF GENITOURINARY DISEASES. By Austin I. Dodson, M.D., F.A.C.S. St. Louis: The C. V. Mosby Co., 1934.

APPLIED ANATOMY; THE CONSTRUCTION OF THE HUMAN BODY CONSIDERED IN RELATION TO ITS FUNCTIONS, DISEASES AND INJURIES. By Gwilym G. Davis, M.D. 9th ed., completely revised by George P. Muller, M.D. Philadelphia, London, Montreal: J. B. Lippincott Co., 1934.

ANNUAL CLINICAL REPORT OF THE GOVERNMENT HOSPITAL FOR WOMEN AND CHILDREN, EGMORE, MADRAS, FOR THE YEAR 1933. Madras: Government Press, 1934.

WEGE ZUR VERHUETUNG DER ENTSTEHUNG UND AUSBREITUNG DER KREBSKRANKHEIT. By Prof. Dr. Bernh. Fischer-Wasels. Berlin: Julius Springer, 1934.

PRACTICAL OBSTETRICS FOR STUDENTS AND PRACTITIONERS. By P. Brooke Bland, M.D., and Thaddeus L. Montgomery, M.D. 2d ed. Philadelphia: F. A. Davis Co., 1934.

HEALTHY BABIES ARE HAPPY BABIES; A COMPLETE HANDBOOK FOR MODERN MOTHERS. By Josephine Hemenway Kenyon, M.D. Boston: Little, Brown, Co., 1934.

CATARACT; ITS ETIOLOGY AND TREATMENT. By Clyde A. Clapp, M.D., F.A.C.S. Philadelphia: Lea & Febiger, 1934.

TUMORS OF THE FEMALE PELVIC ORGANS. By Joe Vincent Meigs, A.B., M.D., F.A.C.S. With a Foreword by Robert B. Greenough, M.D. New York: The Macmillan Co., 1934.

THE CYCLOPEDIA OF MEDICINE. Edited by George Morris Piersol, B.S., M.D., assisted by Edward L. Bortz, A.B., M.D. Vol. xi. Philadelphia: F. A. Davis Co., 1934.

THE SCIENCE AND PRACTICE OF SURGERY. By W. H. C. Romanis, M.A., M.B., M.Ch. (Cantab.), F.R.C.S. (Eng.), F.R.S. (Edin.), and Philip H. Mitchiner, M.D., M.S. (Lond.), F.R.C.S. (Eng.) 5th ed. Vol. i—GENERAL SURGERY. Vol. ii—REGIONAL SURGERY. Philadelphia: Lea & Febiger, 1934.

AMEBIASIS AND AMEBIC DYSENTERY. By Charles F. Craig, M.D., M.A. (Hon. Yale), F.A.C.P., F.A.C.S., Colonel, U. S. Army, Retired. D.S.M. Springfield, Illinois, and Baltimore, Maryland: Charles C. Thomas, 1934.